TEXTBOOK OF
CLINICAL MEDICINE

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Edited by

JOHN W TODD



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Preface

This book was conceived in the belief that certain faults are common in existing medical textbooks The chief of these faults appeared to be (1) The impression tends to be given that the illnesses of most patients can be fitted into one of the precise entities which form the subdivisions into which the books are divided In practice this frequently cannot be done (2) Statements about aetiology tend to be most uncritical Such factors as overwork strain septic foci constipation and in recent years, the stress and strain of modern life ' have been said without sound evidence to be important causes of numerous disorders (3) Whereas specific drugs and surgery have been analysed critically in recent years other less precise remedies such as diet climate, rest exercise and physiotherapy are often advocated for no other reasons than custom or *a priori* speculation (4) Whereas the psychosomatic theory of aetiology has commonly been overstressed in recent years, there is a tendency to overlook the other emotional aspects of bodily disorders These aspects especially with disorders which are fairly benign but frightening to the layman such as hypertension and heart conditions, can be more important than the direct effect of the disorders themselves

It is hoped that these faults are avoided in this book In so far as disorders cannot be put under the heading of a well-defined pathological lesion or at least a clearly recognizable syndrome they have been grouped under such convenient labels as chronic low backache' or dyspepsia of unknown origin ' We have endeavoured not to advance aetiological theories which have no basis and to make the same critical evaluation of diet regime and physiotherapy as of specific drugs

In planning any book of this kind the problem arises as to what to include and what to exclude There is no chapter on dermatology because it was felt that most aspects of skin diseases have but a slender connection with other branches of medicine and because those who wish to study dermatological matters usually go to a specialized textbook There is also no chapter devoted to psychological disorders Patients who are maniacal obsessed paranoid confused or overtly depressed or worried cannot possibly be held not to have psychological disorders The patients with such disorders who present diagnostic difficulties are those whose symptoms are predominantly somatic The difficulties are increased when the patients also have bodily diseases The elucidation of problems of this kind demands not a separate chapter on psychiatry but the integration of the psychological aspects with the other aspects of medicine This has been attempted in the six introductory chapters and where appropriate throughout the book The kind of psychotherapy which can be given by ordinary doctors is moreover indicated for those with bodily diseases as well as for those whose symptoms are wholly of psychological origin

JOHN W TODD

Farnham Surrey

List of Contributors

CLARKE WILLIAM E MD MRCP
Physician and Physician in Charge of Cardiac Clinic Royal Northern Hospital and Highlands General Hospital Physician Hornsey Central and Wood Green and Southgate Hospitals

FORBES JOHN MD, FRCP
Physician the Wrexham Hospitals N Wales

HARDWICK, CHRISTOPHER MD, FRCP
Physician Guy s Hospital

HAWKINS C F, MD, FRCP
Physician United Birmingham Hospitals and Mid Worcestershire Group Lecturer in Clinical Medicine University of Birmingham

KREMER MICHAEL, MD BSC FRCP
Physician in Charge of Nervous Diseases the Middlesex Hospital Physician The National Hospital Queen Square

LEWIS A A G MD, BSC FRCP
Physician, The Connaught Chingford and Woodford Jubilee Hospitals

ST HILL, CHARLES A, MB, CH B
Pathologist Royal Southern Hospital Liverpool Lecturer on Forensic Medicine, Liverpool University Home Office Pathologist, Liverpool area

SCADDING FRANK H MD FRCP
Physician The Middlesex and Brompton Hospitals

THOMAS C C MA MD
Pathologist Farnham Group of Hospitals Surrey

TODD JOHN W MD, MRCP
Physician Farnham Group of Hospitals Surrey

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CHAPTER 1

Aetiology

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The word aetiology when used in medicine has two meanings First, it refers to organisms dusts and other agents which are the immediate cause of diseases Secondly it refers to factors which are thought to be responsible for the development of diseases however caused

THE IMMEDIATE CAUSE OF DISEASES

Some diseases are by definition due to specific organisms. Thus tuberculosis must be due to the *Mycobacterium tuberculosis* and syphilis to the *Treponema pallidum* On the other hand many diseases due to organisms are given the name of some such inflammatory process as pneumonia or meningitis which may be due to *many different organisms*

In practice therefore an organism may sometimes be sought to establish a diagnosis (such as tuberculosis) and at other times having already made the diagnosis by means other than bacteriological an organism may be sought to obtain guidance about prognosis and treatment When no organism can be found this may mean that the patient is free from the suspected disease or that the lesion is not in fact an infection But our methods of studying organisms are far from perfect. The viruses cannot be seen by ordinary microscopy or grown by ordinary culture methods and many bacteria are difficult to isolate and grow or may be outnumbered by other irrelevant organisms The apparent absence of an organism therefore does not necessarily reflect a true absence

The positive error of wrongly attributing some illness *to a particular organism may also be made* for the following reasons (1) The causative organism is wrongly identified (2) The isolated organism is an irrelevant accompaniment of the true organism which is overlooked Alternatively numerous organisms are isolated only one of which *is responsible for the illness* (3) *A non infective* lesion is attributed to an organism which chances to be present on it

These errors occur not only with the individual case In the past certain syndromes were wrongly attributed to particular organisms Influenza was said to be due to Pfeiffer s bacillus it is now known to be due to a virus the Pfeiffer s bacillus being a secondary invader Gastric ulcer disseminated *sclerosis* and many *other diseases now thought to be in no sense infections were attributed to* organisms which had been isolated by some enthusiast.

It was at one time believed that toxins absorbed into the blood stream from local infections in tooth sockets tonsils and elsewhere caused various local and general disorders through the mechanism of the septic focus This mechanism will be considered below (p 4) along with the other factors which are thought to be responsible for diseases giving aetiology its second meaning

Aetiological agents other than organisms which directly cause diseases include trauma dusts and inhaled poisons ingested irritants and poisons skin irritants physical agents (such as heat cold and electricity) and deficiencies of foodstuffs Often it is so obvious these agents are operating that there is no problem of aetiology When a man who has been run *over by a lorry is found to have a fractured* femur the cause of his fracture is overwhelmingly clear But when some of these agents have been operating in small amount for a long time it may not be apparent why those under their influence have developed certain diseases Thus it can be far *from obvious that someone who develops dermatitis* has become sensitive to a substance he has been handling for years

AETIOLOGICAL FACTORS IN THE DEVELOPMENT OF DISEASE

Even when a disease is immediately caused by an organism dust trauma deficiency or other agent aetiological problems usually remain It must be asked why a particular individual has developed an infection whereas others who are equally exposed to the causative organism remain unaffected or

why one man has developed silicosis whereas others who have breathed the same dusty atmosphere have not If a man runs his car into a tree the car s impact with the tree is the *immediate cause* of his injuries But there is still the question Why did the accident occur? The answer may lie in some such extraneous factor as a burst tyre but it may also lie in some quality of the driver Perhaps he was anxious or drunk Similarly the immediate cause of the vitamin deficiency states of the woman with anorexia nervosa is obvious but the important aetiological question is Why has she starved her self? This question may be very difficult to answer

Immediate causes have not been discovered for a high proportion of bodily diseases These include neoplasms the diseases related to arteriosclerosis and other degenerative processes most of the rheumatic disorders peptic ulcer ulcerative colitis and many more The aetiological problem in regard to such diseases is confined to the various aetiological factors which are thought to be respon sible for their development

The number of aetiological factors which have been incriminated rightly or wrongly is very great Among them are heredity diet climate housing overcrowding clothing occupation trauma strain diet exercise (or the lack of it) tobacco smoking and alcohol. Several disorders of body or mind have also been thought to be themselves re sponsible for other bodily diseases they include anxiety and other psychological upsets constipation and septic foci

Such factors may be the immediate cause of dis ease in the sense considered in the last section A diet deficient in vitamin D causes rickets and trauma may cause fractures But it may also be held that a diet which is not poor enough to cause deficiency states may yet be a factor in the aetiology of infections and other diseases and that chills damp and other climatic influences may precipitate colds or rheumatism

Many of these factors are inextricably interrelated with others Thus poverty implies poor housing overcrowding dirt and a monotonous diet Many diseases are much commoner among the poor than among the rich and the contrast between the vital statistics of the rich Western countries and the *peasant countries of Asia is great indeed But it is* a difficult and perhaps impossible task to determine to what extent each of the numerous factors bound up with poverty is responsible for this difference

There is sometimes convincing evidence that one of these factors plays an important part in the aetiology of a particular disease A factor in causing carcinoma of the lung for example is excessive cigarette smoking But frequently it is impossible to incriminate any factor except heredity And the attempt to reach general conclusions about the relative significance of the various factors is apt to *end in vague theorizing of no practical value*

The aspect of medicine about which the public believe they know most is aetiology Every illness must be put down to something—to draughts damp cold poor food a blow a shock or the meno pause which can account for almost any ailment in women between the ages of 35 and 60 A popular factor in the public mind is the unnaturalness of life Men have often dreamed of a distant Golden Age when life was simple and natural and everyone was healthy One hears of the diseases of civiliza tion and of the myth of the healthy savage At present artificial foods are widely thought to be particularly malign Societies spread the gospel that food grown with chemical fertilizers or sprayed with insecticides must be harmful and that white flour ground with steel rollers has had all the goodness taken out of it

Various aetiological factors have had phases of popularity in medical writings At present the psy chosomatic theory is in vogue and some ascribe a large proportion of bodily diseases to psychological causes In the past the septic focus explained numer ous diseases and at another period it was believed that chronic constipation led to intestinal auto intoxication and in this way toxins would circulate in the blood stream and set up various ill effects throughout the body Single diseases have often been attributed on the slenderest evidence to vari *ous causes The common cold is traditionally* brought on by having cold wet feet and in the tropics gastro intestinal upsets are attributed to lying naked under a fan which cools the abdominal skin The theory that cold wet feet cause colds has been largely destroyed by the evidence produced in the Common Cold Research Unit but other similar theories based on no better evidence remain

The Hereditary Factor In addition to obvious congenital defects such as naevi or cleft palate the development of numerous disorders is partly de termined by hereditary factors Many kinds of malignant disease occur with similar frequency throughout all strata of society suggesting that environmental factors are unimportant, and they *may also have a tendency to run in families Even* when a cancer can be related to something external —as carcinoma of the bronchus can be related to tobacco smoking—there still remains the question Why has this individual developed carcinoma of the bronchus yet many others who smoked more heavily and for longer have remained free of it? This question can best be answered by hypothesiz ing a hereditary factor The diseases due to

arteriosclerosis" such as strokes and coronary artery disease are sometimes ascribed to strain overwork and other external factors but their tendency to run in families and their fairly similar incidence throughout all strata of the population suggests they are largely inborn The development of many infections is only partly determined by disease-causing organisms for these may be universally dispersed yet only a few people fall sick of the diseases they cause Some people very rarely have colds it is difficult to explain their immunity on other than hereditary lines

Even such matters as poverty bad housing and malnutrition which are thought to be responsible for much ill health may in the final analysis be related to heredity The man born with some physical or psychological defect tends to fall in the social scale with the result that his living conditions become overcrowded and his food deficient so he develops some disease which he would otherwise have avoided.

Hereditary factors are therefore in a sense all pervading as a cause of diseases But since one is usually helpless in both preventing and treating diseases in so far as they are hereditary this helps little in practice No doubt because of this helplessness there is perhaps a tendency to minimize the importance of hereditary factors On the other hand a hereditary cause for a disease is sometimes satisfying to the layman especially when the disease is to the public shameful The relatives of a lunatic may prefer to attribute his disorder to heredity for which they cannot be held responsible than to his environment for which perhaps they can

The Psychological Factor The theory that many organic diseases are psychosomatic in the sense that they are caused by emotional upsets deserves special attention because of its current popularity Enthusiasts have claimed that few diseases may not, at least sometimes and in part be psychosomatic But there is nothing modern in the idea that bodily diseases may be caused by emotional disturbances Ordinary people have never doubted that this is so When one of their loved ones dies they will not hesitate to ascribe his fatal illness to his self sacrificing labours In the novels of the nineteenth century a miscarriage might be preceded by some violent emotional storm being crossed in love might cause a girl to go into a fatal decline and a shock might be followed by grave or fatal brain fever

Among the diseases which are now often said to be psychosomatic are duodenal ulcer coronary artery disease hypertension asthma ulcerative colitis rheumatoid arthritis many skin conditions and thyrotoxicosis Psychological factors are also said to play a part in the aetiology of many other diseases including diabetes and even some infections such as pulmonary tuberculosis the common cold and recurrent boils

Many of the diseases said to be "psychosomatic" such as duodenal ulcer and coronary artery disease are now diagnosed much more often than they were This increased incidence is often attributed to the stress and strain of modern life" But the increase can at least partly be accounted for by a heightened awareness of these conditions improved methods of diagnosis and in the arteriosclerotic disorders the higher average age of the population Even if there has been a real increase to assume that this must be due to a change in the circumstances of life is surely an example of the *post hoc ergo propter hoc* fallacy It may also be asked whether men do in fact suffer more stress and strain now than in the past if actual times of war are excepted The typical citizen of Britain 100 years ago worked for long hours in most unpleasant conditions for a very small wage and when unemployed ill or old (which he often was) had nothing but the hated Poor Law to help him The citizen of to-day is apparently much better placed Indeed although he is often said to suffer much stress and strain" in other contexts he is told that he is cosseted from cradle to grave by the Welfare State Moreover the amount of stress and strain which a man *feels*—and that presumably is the factor thought responsible for the psychosomatic diseases—does not depend wholly on his external circumstances to a large extent it depends on his temperament

There are also a number of other reasons why the wrong conclusion can sometimes be reached that organic diseases are caused by emotional disturbances

1 Organic disease is often responsible for anxiety and certain diseases said to be psychosomatic such as extensive dermatitis rheumatoid arthritis and ulcerative colitis are so unpleasant that their victims are especially apt to be upset mentally by them The deduction can be made that an emotional upset has caused an organic disease when in fact the disease has caused the upset

2 Psychological disorders are extremely common Such disorders and a subsequent organic disease may in fact be coincidental but the error is made of relating them

3 Some people welcome the partial invalidism made possible by an innocent chronic disease because it enables them to escape from their responsibilities or gives them the sympathy for which they crave The correct observation that a patient has this attitude may be followed by the deduction

which can easily be wrong that this actually caused his illness

4 Emotional factors sometimes provide so wel come an explanation of disease to a patient or his relatives that the doctor is tempted to agree with it if it is suggested A woman whose husband has had a stroke may be consoled by the thought that it was due to his never sparing himself in the service of others

5 *Emotional upsets can cause bodily symptoms* such as weakness nausea palpitation trembling impotence and dyspareunia (*see* p 12) Symptoms of this kind have often been wrongly attributed to such hypothetical organic diseases as fibrositis when the complaint is of widespread pain gas tritis when there are digestive symptoms and myocarditis when palpitation aching in the chest and giddiness are prominent The physician who concludes that patients with these symptoms have psychosomatic diseases is right in his view that the symptoms are of emotional origin His error lies in hypothesizing the pathological changes of fibro sitis gastritis and myocarditis

There can nevertheless be no doubt that emotional factors may play a part in the aetiology of certain organic diseases The relapses of duo denal ulcer are sometimes clearly related to anxiety A similar conclusion can be reached of many attacks of asthma of some skin conditions and some cases of ulcerative colitis But there is little evidence that emotional upsets play a significant part in the aetiology of the arteriosclerotic and rheu matic disorders Coronary artery disease may be closely involved with the emotions for a heart attack is a horrifying experience and emotion may certainly precipitate an attack of anginal pain But this does not justify the frequently heard assertion that the worrying life of a doctor actually causes his coronary arteries to become diseased Even when there are good grounds for the view that emotional factors may precipitate an attack of some disease in certain patients the same may not be true of other patients Many duodenal ulcer subjects seem stable and phlegmatic and deny that the relapses of their disease have followed mental stress

Perhaps the venereal diseases (except when con tracted other than by sexual intercourse) are always in a sense psychosomatic though they are not usually given this name Otherwise there is no justification for giving any disease the unqualified description psychosomatic for this implies that the onset of the disease can be wholly explained by psychological factors The most that can be said is that these factors are sometimes of some rele vance This does not mean that psychosomatic relationships are unimportant for the mind can affect the body and the body can affect the mind quite apart from the aetiology of organic diseases Certain organic conditions which are hardly dis eases themselves may undoubtedly be due some times to psychological factors A common example is thinness which may be due to melancholia mania or anxiety states Obesity too may have a psychiatric basis and some people when distressed drown their sorrows by eating to access The vita min deficiency states of the alcoholic or the subject of 'anorexia nervosa and the skin lesions of dermatitis artefacta can also be called psychoso matic Many bodily symptoms have their origin in the emotions as was noted above The knowledge that he has a bodily disease or unpleasant bodily symptoms may cause a person to become depressed or anxious Finally men may have greatly differing attitudes towards any given bodily disease an ail ment which submerges one may be almost ignored by another

The Infective Focus A few decades ago the theory of focal infection was widely accepted as an explanation of many diseases The rheumatic con ditions such as most kinds of arthritis sciatica and fibrositis peptic ulcer nephritis iritis and many kinds of anaemia were all attributed to septic foci In consequence a common surgical procedure was the removal of septic foci in the tooth sockets cranial air sinuses and elsewhere

This theory is now almost dead It nevertheless deserves mention because its wave of popularity should serve as a warning against the uncritical acceptance of other aetiological theories Many of the diseases such as rheumatoid arthritis and peptic ulcer which used to be attributed to septic foci are now often said to be psychosomatic If the former theory was wrong there should be all the greater caution in accepting the latter

An infective lesion in one place can undoubtedly be responsible for other lesions elsewhere through the dissemination of organisms The subject of re current boils may have a focus of staphylococcal infection in the nose and the organisms on the heart valves of the subject of infective endocarditis may originate in septic teeth This spread of organisms is not the mechanism which was usually hypothe sized under the septic focus theory It was thought that a toxin absorbed from the focus was respon sible for the neuritis arthritis peptic ulcer or other distant lesion Now there is sometimes strong evi dence that a substance arising from an infection in one place is related to pathological changes else where An example is the streptococcal throat infection which so often precedes an attack of rheu

matic fever or acute nephritis" yet the streptococci do not directly cause the swollen joints and carditis or the inflamed kidneys But only a small minority of people develop these sequelae of streptococcal infection so it seems that their tissues have some peculiar sensitivity to streptococcal toxins

There may well be other processes similar to that of streptococcal infection and rheumatic fever or acute nephritis. But it seems most improbable that chronic infective foci from which toxins are absorbed over a long period can cause a recurrent or chronic disease as suggested by the septic focus theory Nor is there good evidence that such foci aggravate the numerous chronic conditions of known or obscure aetiology in whose treatment the *eradication of septic foci used to be and still some* times is recommended

CHAPTER 2

Principles of Diagnosis

JOHN W TODD

THE MEANING OF DIAGNOSIS

According to the *Concise Oxford Dictionary* diagnosis means identification of disease by means of patient s symptoms etc But many symptoms such as headache and exhaustion are often not due to anything which can be called a disease A better definition of diagnosis than that given above is therefore the explanation of the patient s symptoms

Even when symptoms are clearly related to some pathological lesion they cannot be wholly explained by this lesion The imaginative and intelligent patient with a given lesion complains of more numerous and more severe symptoms than does the unimaginative dullard with the same lesion A complete diagnosis should therefore consist of more than a single label representing a disease it should also contain a reference to the state of mind of the subject *With most acute and recoverable conditions* the psychological aspects of diagnosis can for practical purposes be ignored It makes little difference to the assessment and management of a case of acute appendicitis that the patient is of sensitive temperament and constantly groaning or of phlegmatic temperament and lying passively in bed without a murmur With progressively fatal diseases too the organic process is so overwhelmingly important *that a diagnosis consisting of this alone is* adequate

The single diagnostic label becomes incomplete and may be grossly wrong when a patient has a chronic benign organic process If a man with a sebaceous cyst which he is convinced is a cancer is given the diagnosis sebaceous cyst he is being diagnosed wrongly The subject with rheumatic heart disease which interferes little with cardiac function may complain of dizziness exhaustion and palpitation To give him the bald diagnosis mitral stenosis is wrong because this lesion does not cause these symptoms The correct diagnosis should be along the following lines Mitral stenosis causing little cardiac embarrassment occurring in a nervous subject who worries about his heart and has various symptoms of anxiety This diagnosis will naturally be followed by reassurance and an explanation to the patient as to how his symptoms arise

These considerations are insufficiently appreciated Medical students are often given the impression that when an organic lesion has been found and *identified that is the end of the diagnostic process* It is doubtful if the student in a clinical examination in surgery would be given credit for discovering that the patient with a sebaceous cyst is obsessed with the fear that his lump is a cancer The orthopaedic surgeon who operated upon a hysteric with hallux valgus might be angry with the patient for his bitter complaints in the face of assurances that the operation had been entirely successful and the *foot now of normal shape Would he admit that he* had made an error of diagnosis because he had concentrated all his attention on the foot and never gave the possessor of the foot a moment s thought?

THE LABELS WHICH ARE CALLED DIAGNOSES

Pulmonary tuberculosis and migraine carcinoma of the stomach and essential hypertension general paralysis of the insane and uraemia diabetes mellitus and obsessional neurosis hay fever and hallux valgus are all said to be diagnoses But the disorders which these labels describe are of completely *different kinds* Most of them can be classified under the following heads There is no sharp dividing line between these categories and some conditions *can be put into more than one*

1 Aetiological Diagnoses

Common aetiological agents are trauma pathogenic organisms poisons and deficiencies of food mineral salts vitamins or water Diagnoses of this kind therefore include measles plumbism scurvy

and heat exhaustion Since traumatic conditions almost inevitably imply some gross pathological change they are best put under the combined aetiological and pathological diagnoses This is also true of most infections

2 Pathological Diagnoses

Pathological processes are often grouped into neoplasms inflammations and congenital or acquired defects Examples of pathological diag noses are carcinoma of the lung and fibromyoma of the uterus pneumonia fibrositis neuritis and gastritis and cleft palate and patent interventricular septum

3 Combined Aetiological and Pathological Diagnoses

These include pulmonary tuberculosis streptococcal tonsillitis syphilitic aortitis pneumoconiosis fractured femur and traumatic aneurysm

4 Functional Diagnoses

The word functional does not mean here (as it often does in practice) that the disorder is psycho logical It means that there is a bodily disturbance without apparent pathological or psychological basis Idiopathic epilepsy migraine paroxysmal tachycardia and constipation are typical examples

Many epileptic fits are related to some such organic process in the brain as a tumour or a scar from an old injury It may be wondered therefore whether all cases of epilepsy would be found to be organic" if our methods of histological study could be sufficiently improved A similar question may be asked of migraine paroxysmal tachycardia pre mature systoles and other functional disorders But even if in time all these conditions are found to be organic they will still form a distinct group because the relation between the organic focus and say an epileptic fit is of an entirely different nature from the relation between other pathological changes and their clinical manifestations It will still be proper to describe epilepsy as a widespread temporary disturbance of cerebral function precipi tated by an organic focus

Some attacks of these functional disorders—in particular migraine—may apparently be precipi tated by emotional causes But this observation no more justifies the removal of migraine (in so far as it is of emotional origin) from this group of con ditions than does the discovery that epilepsy is organic The relationship between the psycho logical upset and migraine remains of a different nature from the relationship between such upset and tachycardia exhaustion impotence and the other bodily symptoms which are immediately due to the emotional state

5 Descriptive Diagnoses

Under this head may be put scoliosis pes planus genu valgum and similar conditions There is no sharp dividing line between these and the patho logical diagnoses Scoliosis may be secondary to poliomyelitis and then the unqualified diagnosis scoliosis" would be wrong rather should the patient be said to have old poliomyelitis of the erector spinae muscles Even when the defect gradu ally develops in the course of years without appar ent cause it may be thought that the defect itself —the flat foot or the knock knee—should be called a pathological change This is perhaps admissible though such changes are of a different nature from those usually said to be pathological

Many skin conditions are probably best placed in this category The expert dermatologist can often do no better than describe the appearance of the skin lesions in such terms as diffuse psoriasoform eruption with impetigenization and lichenification Such conditions reveal histological changes it is true but these are usually of a non specific kind and less characteristic than the general appearance of the skin

6 Symptomatic Diagnoses

In general a symptom is in no sense a diagnosis yet in practice several symptoms have attained the stature of diagnoses A common example is angina pectoris This term implies that the heart is diseased and it could be replaced by a pathological diagnosis but the pain is so supreme a feature of the malady that the symptomatic diagnosis shows no sign of dying Other examples are lumbago sciatica and facial neuralgia These terms too imply patho logical processes but the nature of these processes is sometimes obscure and opinions about them have changed from year to year This obscurity is no doubt partly responsible for the popularity of these diagnoses

7 Biochemical Diagnoses

These include uraemia alkalosis hypoglycaemia and salt depletion All imply a pathological process or some such aetiological agent as excessive sweat ing combined with a small salt intake They should usually be combined therefore with aetiological or pathological diagnoses A patient may be said to have uraemia due to chronic nephritis or hypogly caemia due to insulin over-dosage Perhaps diabetes mellitus should be put in this category Its patho logical basis is obscure and its supreme feature is the biochemical disturbance

8 Psychological Diagnoses

The psychological disorders can be divided into those due to organic disease of the brain and those thought to be disorders of the mind itself developing in a structurally normal brain Among the former are senile dementia and syphilitic dementia paralytica These can alternatively be given pathological or aetiological diagnoses The diagnoses which are thought to reflect purely mental disorders include anxiety neurosis obsessional neurosis manic depressive psychosis and schizophrenia Some of these such as obsessional neurosis are descriptive diagnoses and reflect the predominant psychological abnormality Others such as puerperal insanity or menopausal depression imply an aetiology

Psychological disorders may be responsible for various bodily manifestations such as weeping palpitation exhaustion impotence and paralysis In the past such manifestations were often attributed to hypothetical organic disease of the region from which they arose now when their true nature is appreciated they are often said to be functional But epilepsy migraine and the other conditions which were put under the heading of functional diagnoses are in no way similar to such conditions as these Whether or not psychological disorders have somatic manifestations it is best to give them psychological diagnoses and not describe them as functional

A similar question may be asked of the psychological disorders as was asked of the functional disorders Thus if our methods of histological study were sufficiently improved would it not be found that there were no disorders of the mind developing in a structurally normal brain but that all psychological disorders were organic? To many this is an attractive hypothesis and superficially there perhaps seem to be reasons for supposing it is true The condition of the subject with syphilitic dementia paralytica which is undoubtedly organic differs little from that of the subject with advanced schizophrenia which is supposed to be a mental disease Yet there are other and stronger grounds for rejecting the general hypothesis even if it is true of some varieties of mental disorder The normal person who suffers some grave psychological trauma may develop such symptoms as insomnia irritability difficulty in concentration and exhaustion It can hardly be denied that the essential cause of these symptoms is psychological They are precisely similar to those suffered by the person who is given the diagnosis of anxiety neurosis If they are psychologically determined in the first case it is difficult to argue that they are organically determined in the other though it is no doubt possible that the difference between the normal person who develops these symptoms when subjected to gross psychological trauma and the anxiety neurotic who develops them for apparently trivial reasons is in the final analysis to be explained by a difference in the structure of their brains

Erroneous Aetiological and Pathological Diagnoses

The most satisfactory diagnoses for bodily diseases are the aetiological and the combined aetiological and pathological The other categories are more or less unsatisfactory and the view may be held that some can hardly be called diagnoses

There is a natural desire therefore to make aetiological and pathological diagnoses wherever possible and such diagnoses as acute lumbago or chronic dyspepsia may be condemned This desire has unfortunately been responsible for hypothesizing aetiological agents and pathological changes which have no reality

In the past many diseases such as the various rheumatic disorders were wrongly attributed to organisms especially through the mechanism of the septic focus More recently many syndromes were wrongly attributed to fanciful pathological changes It was hypothesized that patients with pain and areas of local tenderness in the back had fibrositis and textbooks described the aggregations of fibroblasts round celled infiltration oedema and other pathological changes of this condition Patients with chronic dyspepsia were said to have chronic gastritis and those with persistent dull pain in the right iliac fossa to have chronic appendicitis

Both in the past and at present perhaps the commonest manner in which aetiological and pathological diagnoses have been wrongly made has been by improperly attributing symptoms to a benign abnormality Few men are free of some imperfection and it is easy to deduce that the imperfection is the cause of the symptoms The patient with headache may be found to have a raised blood pressure a deflected nasal septum radiologically opaque cranial air sinuses and astigmatism He may therefore be given one of four diagnoses—and innumerable people have been given such diagnoses—yet all four are equally wrong The chronic dyspeptic may be shown radiologically to have visceroptosis gall stones or diaphragmatic hernia and by gastric analysis to have achlorhydria But the dyspepsia

may be unrelated to all these abnormalities and have some other cause or no apparent cause (It is not of course suggested that all the abnormalities mentioned are never responsible for symptoms Sinusitis gall stones and astigmatism often cause symptoms and make correct diagnoses)

Not only does the individual doctor have an understandable desire to make aetiological and pathological diagnoses in many circumstances he is guided along the same road by authority He is told that he should not attribute deaths to such vague conditions as cardiac failure uraemia or senility but should describe the underlying pathological state He therefore writes on the death certificate myocardial degeneration or cerebral arteriosclerosis although there may be no evidence that the myocardium is degenerate or the cerebral arteries arteriosclerotic The medical officer in the Services may be admonished for discharging patients from hospital with pyrexia of undetermined origin or diarrhoea If on the other hand he writes down dengue fever or colitis all will be well although there may be no evidence for such diagnoses

The Correct Aetiological and Pathological Diagnosis

Even if the psychological aspects of diagnoses are ignored and even if the only patients studied are those affected by gross pathological lesions or such aetiological agents as pathogenic organisms or poisons it may be impossible in practice to reach a confident conclusion The most searching clinical examination by the best clinician may not produce sufficient data particularly in the initial stages of an illness Investigations and later developments may in time provide the answer but sometimes a patient will recover without its ever being known what was the matter with him Alternatively he may continue to be an obscure problem until he dies

A patient may develop fever with only such general symptoms as malaise sweating and headache and no signs There are numerous possible causes of the trouble including enteric fever brucellosis pyelitis infective endocarditis and Hodgkin s disease but there are no data to give a clear lead The problem here is not so much What is the diagnosis? as Should we await developments should we do some investigations (and if so which investigations) or should we give treatment in the hope that there is a causative organism sensitive to an antibiotic? The patient with an acute abdomen may reveal findings which are compatible with a number of diagnoses The problem he presents is Should we do an immediate laparotomy and if so where should the incision be made The middle aged man with a slowly developing spastic paresis of the legs may have disseminated sclerosis a tumour of various kinds spondylosis or other conditions but even with exhaustive clinical examination and investigation by lumbar puncture and myelography it may be impossible to decide which of these conditions is present Even after the lapse of many years the matter may still be in doubt

In such circumstances as these a physician may guess at some diagnosis and if subsequent developments confirm his guess he may seem to have performed a remarkable *tour de force* In fact he was wrong because he reached his conclusions from insufficient data The correct provisional diagnosis should have been given in the following terms Several conditions could explain the findings in this case Of these probably the most likely is *A* because it is common but other possibilities are *B* *C* and *D* while *E* and *F* are also conceivable

Stories are sometimes heard of a great physician of the recent past who would be taken to a case which had baffled the lesser men in the hospital After a few terse questions and a searching physical examination he would pronounce the diagnosis which would invariably turn out to be correct and would usually be confirmed later in the post mortem room No doubt there are circumstances in which one man can *rightly* make a confident diagnosis which others had failed to make perhaps because of his previous experience of similar cases or because he had noted the existence of some significant finding which they had overlooked But the above considerations suggest that it is very often right to be uncertain as to the diagnosis and very often wrong to be dogmatic about it We do not hear the following 'The great man was shown a case which the senior registrar had diagnosed as a *A* the junior registrar as *B* the senior house physician as *C* and the junior house physician as *D* After studying the findings he concluded that they were all wrong because there were not enough data to reach a diagnosis though any of their guesses might turn out to be right Perhaps this kind of story more often reveals greatness than does the other kind

The correct diagnosis in any circumstance is then a description of the various possibilities which could account for the available data And the best diagnostician is he who makes a confident diagnosis when there are grounds for it but refuses to make more than a provisional diagnosis when there are not

THE NEED FOR DIAGNOSIS

Even when it is possible to reach an exact aetiological or pathological diagnosis this is not always helpful since diagnosis is not an end in itself but the means to an end Its chief object is to provide indications for treatment A second object is to assess prognosis a third is to tell the patient what is the matter with him Occasionally there may be a fourth object—to benefit others than the patient This is relevant to certain infections for irrespective of the effect of diagnosis on the patient it may prevent others who come in contact with him from developing the infection A diagnosis may also advance medical knowledge and therefore possibly aid in preventing or curing some disease in the future

There are all degrees of precision in reaching aetiological and pathological diagnoses *Congenital* heart disease is an indefinite pathological diagnosis Patent interventricular septum is more precise A description of the exact shape and size of the aperture in the septum and of the character of its walls give the greatest possible degree of precision Pneumococcal lobar pneumonia is an aetiological and pathological diagnosis If the type of pneumococcus is identified the aetiological aspect is made more exact Bacillary dysentery may be divided into the shiga flexner boyd sonne and other varieties

The attempt to reach a broad aetiological or pathological diagnosis such as malaria or congenital heart disease is nearly always right But the objects of diagnosis can sometimes be achieved without a high degree of precision The treatment of a patient with bacillary dysentery is not influenced by knowledge of the type of organism responsible On the average cases of shiga dysentery are more severe than the others but the prognosis in the individual case should be reached on clinical not on bacteriological grounds The patient with widespread secondary deposits is not helped by investigations to determine the site of origin and the pathological type of the growth unless the trouble arose in the prostate or breast Otherwise it is already known that there is no effective treatment and that the prognosis is hopeless

The degree of diagnostic precision required varies from time to time according to the available treatment In olden days there was so little effective treatment that diagnosis except for prognosis and the information of the patient rarely mattered *Until recently there was no need to identify the* precise congenital heart lesion since nothing radical could be done and the prognosis was best determined not by the nature of the lesion but by the functioning capacity of the heart as a whole Now that effective operations can be done for some congenital heart lesions their identification has become most important The failure to diagnose tuberculous meningitis (except from the angle of prognosis) used not to matter now it matters greatly On the other hand in the pre *sulphonamide days* something was gained by typing pneumococci from cases of pneumonia because specific sera were available for each type This degree of precision is no longer necessary because all these sera are inferior to the anti bacterial drugs But testing the sensitivity of the pneumococci to various of these drugs may now be relevant

CHAPTER 3

Means of Diagnosis

JOHN W TODD

SYMPTOMS

Nature and Basis

WHEREAS a high proportion of patients reveal no physical signs and no abnormalities by special methods of investigation nearly everyone who seeks medical advice has symptoms Although most symptoms are unpleasant sensations some manifestations usually described as symptoms such as amenorrhoea and constipation are in themselves by no means disagreeable they are complained of because they are feared to be of serious significance The reason which brings the woman with amenorrhoea to the doctor is the suspicion that she is pregnant or the fear that something is wrong

Many of the true symptoms have a positive quality because they cannot be forgotten or ignored Among them are pain nausea vertigo depression and anxiety Other symptoms such as blindness deafness and paralysis are not in the same sense actively unpleasant men frequently close their eyes to the sights of the outside world by choice They are therefore of a negative kind and are disliked because they prevent people from taking part in activities They tend to be associated especially when they develop suddenly in adult life with the positive symptoms depression and anxiety The blind man is not so much to be pitied because of his blindness as because of his state of mind if he were always cheerful there would be no need to pity him

The unpleasantness even of a positive symptom does not wholly lie in the feeling itself It may lie rather in the anxiety and depression it causes Persistent pain is always worrying for the subject of it must wonder if he will have it until he dies Pain depression and anxiety may also be related in a less direct manner for the man in pain may know what is its cause his knowledge rather than the actual pain making him depressed and worried Depression is indeed the symptom beyond all others which men wish to lose

Apart from this mechanism by which bodily symptoms cause mental symptoms all bodily symptoms are partially mental The severity of pain does not wholly depend on the nature of the organic process underlying it it also depends on the mind of the victim The man of sensitive temperament may suffer great pain from some injury an apparently identical injury may cause little pain to the unimaginative and phlegmatic subject Any individual is more pain sensitive at some times than at others When excited or elated he may hardly notice some injury which he would find agonizing when depressed or worried After a game of football a player may notice bruises which he does not remember receiving Among a ward of badly wounded soldiers there may be hardly a complaint of pain The patients are elated to be alive and to be released from the horrors of battle have no financial worries and look forward to an early reunion with their families whom shortly before they feared they would never see again In a ward of men with injuries of a similar gravity sustained in civil life large doses of analgesics will be needed for their injuries did not come as a release but as an unexpected tragedy

Interpretation of Symptoms

The caus of many bodily symptoms is easily discovered for they indicate some local lesion An ache in the gums leads to the finding of a carious tooth a pain in the finger leads to the finding of a whitlow Other bodily symptoms such as palpitation accompanying excitement and anorexia following profound grief are as obviously due to psychological causes

But the cause of many symptoms may remain obscure after exhaustive examination and investigation There may even be difficulty in deciding whether they are due to an organic lesion or to

psychological disorder As has just been pointed out the severity of a symptom due to an organic lesion depends on the state of mind of the subject as well as on the nature of the lesion Strictly there fore the distinction to be drawn is between symp toms partly due to an organic lesion and those wholly due to psychological upset though in prac tice the psychological aspects of organically deter mined symptoms can often be left out of account

The decision as to whether bodily symptoms are organic or psychiatric is often thought to be most important and incredible efforts may be made in an effort to solve the problem The error of con cluding that a patient s symptoms are hysterical psychological or purely functional when in fact he has an organic disease seems to be considered far worse than the opposite error of wrongly attributing symptoms to some organic disease when in fact they are wholly psychiatric If the former error is responsible for the failure to give a remedy which saves life or prevents prolonged illness it is undoubtedly serious but otherwise it matters com paratively little

That many bodily symptoms are due to psycho logical causes is obvious The very words of the English language indicate that the heart is the seat of the emotions People speak of affairs of the heart when they mean affairs of love a man s heart is said to rule his head when his feelings are stronger than his reason and someone who has suffered a tragic experience is said to be broken hearted Familiar phrases also illustrate how the mind can upset other parts of the body for we talk of being sick with grief speechless with rage and of trembling with fear And people are said to lose their appetites when crossed in love to vomit with disgust to develop diarrhoea from anxiety or to blush with shame

But the dislike of attributing bodily symptoms to psychological causes and the fear of wrongly con cluding that a patient is neurotic have been respon sible for innumerable false organic diagnoses In the recent past such mistakes were more frequent than at present The complaints of palpitation dizziness precordial aching fatigue and sighing respirations would lead to such diagnoses as strained heart tired heart disordered action of the heart fatty heart cardiac debility myocarditis and even angina pectoris or valvular disease of the heart. In the First World War vast numbers of men were invalided from the Army with diagnoses of this kind When nausea anorexia abdominal discomfort and other abdominal symptoms were prominent such diagnoses as visceroptosis and other ptoses adhesions liverish ness intestinal auto intoxication gastritis hyper chlorhydria and colitis were popular Those with the chief complaints of weakness tiredness being run down and other vague symptoms were often said to be anaemic Whatever the symptoms they were often attributed to focal sepsis and such diag noses as apical infection of a tooth and chronic cervicitis would follow Even impotence frigidity dyspareunia and other sexual symptoms were attri buted to inflammation of the seminal vesicles lack of secretion from Bartholin s glands or a small vagina as if the relations between the sexes were an unemotional and impersonal matter Perhaps the only somatic manifestation of psychological origin not attributed to organic disease was weeping for women so affected were not referred to the ophthal mologist to be given the diagnosis of chronic in flammation of the lachrymal glands

Although there is now a greater willingness to admit that many bodily symptoms have psycho logical causes the belief is still common that this conclusion should be reached only as a last resort Over and over it is said or implied that symptoms should only be considered psychiatric or func tional when every possibility of organic disease has been eliminated This doctrine of diagnosis by ex clusion is wrong for the following reasons

1 A symptomless organic disease may be present in a patient whose symptoms are of emotional origin Symptomless diseases are common examples are rheumatic heart disease gall stones and chronic nephritis in its latent stage Symptomless defects such as flat feet scoliosis visceroptosis and vari cose veins are even commoner Those who follow this doctrine must wrongly attribute emotional symptoms to such diseases or defects An organic disease may alternatively be only partially respon sible for symptoms which are predominantly psychiatric To complicate the issue further the man with certain organic diseases—typically those affecting the heart—is especially liable to be upset mentally and consequently to have emotional somatic symptoms

2 Symptoms may be due neither to a demon strable organic lesion nor to psychological causes Such symptoms include much headache backache and bellyache Even well defined syndromes includ ing idiopathic epilepsy migraine and paroxysmal tachycardia have no known pathological basis they were included in the category of functional diag noses considered above (p 7)

3 It may be impossible to exclude certain organic diseases by any method short of exploratory opera tion—and even that may be unsuccessful Among them are carcinoma of the body of the pancreas cerebral glioma and coronary artery disease The doctrine of diagnosis by exclusion therefore

applied to the symptoms of diseases such as these will lead to the wrong conclusion that they are of psychological origin

This conclusion should indeed always be reached on positive not negative grounds The chief positive ground is the demonstration of a clear relationship between the symptoms and the mental state To make this demonstration the patient as a whole with his problems hopes and fears should be studied as well as his presenting symptoms In this way it may become apparent that his symptoms worsen when his anxieties grow and improve when they diminish The subject with cardiac symptoms may be worried about his work Whenever he is about to have an interview with an important person he develops palpitation aching in the chest sweating trembling unsteadiness and difficulty in breathing Exertion on the other hand does not unduly distress him

Many somatic symptoms particularly suggest a psychological origin Persistent impotence and dyspareunia are nearly always psychological though temporary dyspareunia may be due to local lesions Weeping is so characteristically emotional that patients do not so much complain of it as of the melancholy responsible for it Palpitation sighing respiration or difficulty in filling the lungs general bodily weakness sensations of pressure on top of the head or of a tight band round the skull and trembling are also as a rule psychological And in most cases very little inquiry is needed to determine whether or not such symptoms have their origin in the state of mind if so they will be associated with such mental symptoms as constant anxiety tenseness irritability or depression

By contrast other symptoms strongly suggest an organic origin Examples are precise and localized pain of short duration cough expectoration effort dyspnoea vomiting and weakness or paralysis of individual limbs

The number and duration of symptoms shed useful light on their origin in general the larger their number and the longer their duration especially when continuous the more likely it is that symptoms have their origin in the mind Frequently the patient with psychological disorder has symptoms arising from most parts of the body and such general symptoms as weakness and exhaustion as well He may complain of one or a few symptoms ignoring others for a history is often determined by a patient s opinion as to what is the matter with him Leading questions may therefore be needed before concluding that symptoms are in fact few or solitary The patient s description of his pain is often useful Absolutely continuous pain lasting for months or years strongly suggests a psychiatric origin especially when it is widespread and symmetrical

The decision as to whether bodily symptoms are organic or psychiatric should therefore be reached by analysis of the symptoms themselves Moreover in this way certain organic diseases can be absolutely excluded as the cause of the symptoms The story of persistent abdominal symptoms which have not changed for 10 years cannot be due to say malignant disease A patient with this story may conceivably have malignant disease (for this can be symptomless for a time) but the failure to discover it is no more reprehensible than is the failure of the dermatologist to discover that the patient with athlete s foot has a cerebral glioma The study of physical signs and the use of special investigations to elucidate the cause of symptoms should come after the decision has been reached from the history that the symptoms may be at least partly due to an organic process

PHYSICAL SIGNS

Types

Many signs are clearly abnormal phenomena among them are lumps skin eruptions râles and pleural rubs Other signs are merely variations of manifestations which are the properties of all men they include tachycardia bradycardia hypertension obesity and leanness

The abnormal signs are usually due to some pathological process and are of great assistance in reaching diagnoses Their interpretation is in most cases fairly simple But there are certain signs apparently belonging to this group which are not necessarily due to disease A common example is the systolic murmur The significance of this sign is often doubtful but it may arise from a normally functioning heart and is compatible with a normal span of life

When studying the manifestations which are variations from normal it should first be decided whether they should be described as signs at all This may be difficult for they vary greatly among healthy men They tend therefore to be ambiguous But some of these manifestations such as the knee jerks and pupillary reflexes are bilateral When the findings are equal on the two sides the problem whether or not there is a significant variation from normal is the same as arises in the study of the

pulse rate or the height But when there is a difference between right and left the situation is greatly changed it may be clear that a knee jerk is impaired after comparing it with its fellow though no such conclusion could be reached from one knee alone These signs due to differences are often just as definite abnormalities as are lumps rubs and rashes and they should be placed in the abnormal group not in the group of variations from the normal

Appreciation

Most of the signs which are variations from normal offer no difficulty of appreciation anyone can see that a man is unduly fat thin tall or short or that his pulse and breathing are rapid or slow But there used to be a widespread belief that the appreciation of many signs both among the abnormal group and the variation from normal group is a difficult art which could be perfected only by years of patient training of the senses Stories were circulated of *great bedside masters whose acuity of hearing* sight or smell enabled them to detect signs beyond the powers of appreciation of ordinary men One of these masters would delicately perform light and heavy percussion over the praecordium and thereby demonstrate the size of the heart A second would detect the slightest impairment of percussion note at one lung apex with hardly perceptible flattening of the contours and an occasional râle and subtle changes in the breath sounds (and he might then de*duce that the patient had pulmonary tuberculosis)*

There are few who would now dispute that these ideas are altogether false They could be held only at a time when the final court of appeal was the opinion of the physician in charge In 1900 it was not possible to prove the physician wrong who demonstrated by percussion the size of the heart the present day physician who did the same would be ridiculed measurements taken from X rays being used to show how wide of the mark he was The *valuable physical signs are those which are striking* and whose characteristics can be agreed upon by any number of observers The very fact that one observer is unable to confirm the presence of a sign discovered by another should always give rise to doubt as to its reality The minutiae of physical signs—the roughening of the first heart sound the increased area of splenic dullness the equivocal plantar response the slight murmur—are rarely of more than doubtful significance and should usually be ignored

Discovery

Although the valuable signs are the striking and easily appreciated ones they are frequently overlooked and anyone can remember occasions when he failed to notice some striking sign Such failures may be thought avoidable and that if patients were always examined thoroughly enough obvious signs could not be missed This is true but in fact patients are not always examined even by most painstaking physicians with sufficient thoroughness

The common reason why signs are not discovered is that the diseases which cause them are not suspected Indeed signs can be overlooked which are so obvious that they must have been seen—seen but not noticed because the attention is being drawn to other matters For example a myxoedematous patient becomes mentally confused His wild behaviour immediately directs attention to his brain and the conclusion is reached that he has an acute confusional state (which is true) and he should therefore be certified Yet the signs of myxoedema are so obvious that had the physician thought of the possibility of myxoedema he would immediately have noticed them A patient reveals the classic picture of cerebral tumour His C N S is examined with extraordinary thoroughness and electroencephalography and air ventriculography are carried out The signs of a primary carcinoma of the lung or of secondary deposits in the supra-clavicular glands may never be noticed A woman who gives a history of rheumatic fever many years before complains of increasing effort dyspnoea and swelling of the ankles An apical diastolic murmur is discovered and the obvious diagnosis of rheumatic heart disease with mitral stenosis is reached But the signs of anaemia—or rather the blood picture as the signs are inconclusive—are never sought yet the anaemia bears a greater responsibility for the symptoms than does the cardiac lesion

Although the way to discover signs is to make a conscious search for them cases differ so widely that no general instruction can be given as to how it should be done Knowing where to look is one of the fruits of experience Frequently it is obvious that a particular diagnosis is probable the signs of it are immediately sought and discovered and further search would bring no further significant

signs to light Errors arise when something unusual is happening—when a rare disease is present when there are uncommon manifestations of a familiar disease or perhaps most of all when two diseases occur together It is sound doctrine (except in the tropics) not to diagnose two independent acute diseases at the same time but two or more chronic diseases or an acute disease with a chronic disease such as acute appendicitis and chronic bronchitis not uncommonly occur together

Interpretation

There are two stages in interpreting signs first deciding what is the cause of the sign and second deciding whether this cause is responsible for the symptoms Sometimes a double error of interpretation is made with a single sign A patient complains of palpitation aching in the chest giddiness and pressure on top of the head he is found to have an apical systolic murmur The deduction may first be made that this sign is due to mitral regurgitation and next it may be concluded that the symptoms are due to this lesion Both these conclusions are wrong A systolic murmur alone is insufficient justification for diagnosing mitral regurgitation and that lesion does not cause such symptoms (which are those of an emotional disturbance)

The importance of the first stage of interpretation is universally recognized but less attention may be paid to the second stage Too often is it wrongly assumed that some lesion is responsible for the symptoms and too often are diagnoses made which are correct in the sense that the conditions thought to be present are present but are wrong because they do not explain why the patients feel ill The patient with essential hypertension complains of "flushings giddiness pressure on top of the head and other emotional symptoms which are either unconnected with the blood pressure or related to it only because his knowledge of his high blood pressure is a source of anxiety The patient with an irreducible inguinal hernia may have vomiting spasmodic abdominal pain and other manifestations of intestinal obstruction which are due not to the hernia but to colonic carcinoma

The somatic manifestations of psychological origin as well as causing confusion in the second stage of interpretation may also be responsible for errors in the first stage Emotional upsets can cause tachycardia hypertension blushing tremor excessive sweating and other signs Many patients with signs of this kind have wrongly been given such diagnoses as myocarditis strained heart and thyrotoxicosis The approach which avoids these errors was described above (p 12)

Interpreting signs may be difficult because of the paucity of our knowledge of the diseases which cause them Many of the rheumatic" disorders are responsible for problems of this kind A patient complains of low backache and is found to have tenderness in the region of the sacro iliac joint and tender nodules These signs have been freely interpreted as due to sacro iliac strain fibrositis lumbo sacral back strain " and other entities but evidence to support such interpretations is lacking Even when the doctor is willing merely to describe an attack of backache as backache (or lumbago) or an attack of stiff neck as stiff neck the patient may feel that he has been cheated If on the other hand he is told that he has rheumatic myositis and fibrositis or subacute interstitial fascitis he may be better pleased Some may defend the use of such meaningless jargon to please the patient no one can defend it if it also deceives the doctor

SPECIAL INVESTIGATIONS

Frailty of Investigations

In the days before investigations the final diagnostic court of appeal was the clinical opinion The present situation is very different The most junior student and even the layman who reads the medical articles in magazines now knows that the five senses and a stethoscope are not always enough (and they may know this even in circumstances when the five senses and a stethoscope are quite enough)

Indeed less attention now tends to be given to the clinical findings than to the results of investigations One reason for this is what G W Pickering calls the fascination of machines As year succeeds year says Pickering some new physical or chemical technique and some new and elaborate machine is applied to the study of disease The machines and techniques are often so complex that he (the practising doctor) cannot understand them He has to take what they tell him on trust That physical signs may be absent or misleading is easily and early learnt the frailty of machine provided answers is less obvious Even the doctor who is aware that machines are not infallible may feel compelled to order an investigation for no other reason than to satisfy the patient The statement that he is free of duodenal ulcer because the history does not

suggest this condition may leave the patient dissatis fied the statement that an X ray revealed no ulcer will usually be accepted as proving that there is no ulcer

Investigations also yield objective criteria The shadow on an X ray film the notched R wave in an electrocardiogram or the haemoglobin of 10 g/100 ml have the appearance of concrete *evidence* whose reality cannot be questioned Symptoms by contrast are commonly so vague that it is hard to be sure what the patient s complaints are and if the history is apparently definite it is still by com parison with a blood urea of 150 mg/100 ml or a positive occult blood test on the faeces an intangible thing Many physical signs do not it is true have this drawback a raised temperature or a diastolic murmur are just as objective and satisfactory as are the results of investigations The symptoms then rather than the clinical findings as a whole are apt to be minimized by comparison with the investiga tions

Yet investigations are often valueless or mislead ing for the following reasons

1 A negative investigation frequently proves nothing Most lesions of the alimentary tract such as carcinomas of the stomach or colon do not neces sarily cause definite abnormalities on the X ray film The organisms of disease which are in fact present cannot always be isolated in the laboratory Haemorrhagic lesions in the upper alimentary tract are not always responsible for a positive occult blood test on the stools On the other hand some negative investigations can exclude certain diseases in very high probability A normal pyelogram ex cludes hydronephrosis A normal haemoglobin figure excludes anaemia (provided that the patient *is not in a state of shock or suffering from a dis* ease causing marked haemoconcentration) Urine free of pus probably excludes an open (though not a closed) urinary tract infection A normal blood urea figure excludes chronic nephritis with nitrogen retention

It is too often wrongly assumed that a particular investigation will exclude a particular disease This error is especially common when there is no alterna tive method of reaching the truth Thus whereas the conclusion that a carcinoma of the stomach may cause no X ray changes is easy to reach (for laparo tomy or future developments will reveal conclusive evidence of carcinoma) *duodenal ulcer provides* a very different problem Future developments may provide no guide and in doubtful cases—and it is then that the difficulties arise—there is usually no question *of doing* a *laparotomy* Occasionally it may be possible to prove that a barium meal X ray has failed to reveal a duodenal ulcer because the patient perforates soon afterwards but to establish a figure giving the proportion of duodenal ulcers which are missed by radiography is not possible Nor can it be *concluded that* a *normal electrocardiogram* no matter how many leads are used will fail to exclude a cardiac infarct in a stated percentage of cases A normal chest X ray does not absolutely exclude pul *monary tuberculosis since a very small tuberculous* lesion causes no identifiable shadow Nevertheless the practical question here is Can a patient s symptoms be due to a tuberculous lesion so small *that it produces no shadow in a number of techni* cally excellent X ray films? This question should perhaps be answered in the negative but it is impos sible to be sure Following up large numbers of cases *may provide further evidence pointing* one way or the other but since a tuberculous lesion may in time heal completely there can be no certainty about this matter

That the failure to find an organism does not exclude a particular infection is sometimes obvious A throat swab which grows no pathogenic organisms cannot prove that tonsillitis is absent since the swollen and acutely inflamed tonsils can be seen and the tender enlarged cervical glands can be felt But too much weight is often given to the apparent absence of organisms Thus although it is widely realized that it may be difficult to find the *Entamoeba histolytica* in the stools of patients with alimentary amoebiasis it is still assumed that the persistent absence of this organism excludes the dis ease The future course of events provides no cer tain guide since the disease *may clear up* spontaneously The patient may therefore need lessly suffer prolonged discomfort from amoebiasis which is wrongly attributed to colitis and which *could have been avoided by anti amoebic* drugs

2 The investigations which produce figures such as blood counts and chemical analyses of the blood or cerebro spinal fluid are often very inaccurate Estimations done on the same specimen in different laboratories may show astonishing differences and sometimes there are considerable differences when investigations on a specimen are repeated in the same laboratory Yet figures appearing on an official form bearing an imposing signature give a strong impression of exactness and these great in accuracies are easily forgotten

When the result of a single investigation is being *considered this technical source of error* usually matters little since it can hardly show a gross abnor mality when none is present (and the gross abnormalities are the important ones) A patient will not wrongly be shown to be markedly anaemic if he is not anaemic or to be uraemic if his blood urea is normal But when conclusions are being

drawn from changes in the results of investigations it is very easy to be led astray The error in red cell counts for example is so great that a drop from 5 million to 4½ million means nothing

Variations in laboratory figures are not wholly attributable to the technique of the investigation they may also be due to physiological changes in the patient. Some chemical constituents of the blood such as the sugar are constantly changing and the number of white blood corpuscles varies greatly from hour to hour There are also considerable changes in the haemoglobin level perhaps up to 10 per cent. Even if therefore technical errors have been excluded by doing repeated estimations of haemoglobin on the same sample and achieving virtually identical results it cannot be assumed that a fall of 10 per cent in the haemoglobin level is significant.

Finally there is the human error A laboratory specimen may go through many hands and yet more hands may be involved in assessing and recording the result Somewhere in the chain a mistake may occur A label with the name of another patient may be attached to the specimen some foreign material may have found its way into the apparatus vitiating the result a mistake in calculation may be made the secretary may misread the figures and type them wrongly and the pathologist engaged in signing numerous reports may fail to notice that a result looks peculiar If a result is wildly wrong the clinician will easily suspect that someone has blundered but if the erroneous result is compatible with the other findings it may have unfortunate consequences Such errors rarely occur with the clinical findings The histories of two patients can hardly be mixed and a physical sign in one man can hardly be attributed to another

Interpreting Investigations

There are two stages in interpreting investigations just as there are in interpreting physical signs The first stage is deciding the cause of the finding the second stage is deciding whether this cause is responsible for the symptoms and is identical with the second stage of interpreting physical signs

Errors in the second stage of interpretation result in those erroneous aetiological and pathological diagnoses which are discussed above (p 8) Thus X ray findings are correctly attributed to sinusitis or diaphragmatic hernia but the symptoms are wrongly attributed to these conditions (It is not of course suggested these conditions are never responsible for symptoms)

The first stage of interpreting investigations—deciding what is the cause of the finding—presents such an enormous variety of problems through differences in the circumstances that sound generalizations are difficult to reach Sometimes the interpretation is obvious as when an X ray shows a fracture gall stones kidney stones or a hydronephrosis At other times the finding is so indeterminate that no useful conclusion can be drawn Nevertheless one generalization with a universal application can be made This is similar to that already made about physical signs (p 14)—namely great caution should be exercised in drawing deductions from minor variations from the normal If a shadow on a chest radiography is very small it is hardly possible to be sure of its significance the right course is to ignore it, to take a further film after an interval or to take special views of the suspicious area If the haemoglobin figure is 85 per cent anaemia should not be diagnosed If in the urine there are merely occasional pus cells it should not be assumed that there is urinary infection Spasm of the duodenal cap seen radiologically is insufficient to diagnose duodenal ulcer A blood urea figure of 45 mg/100 ml does not mean (in the absence of non renal factors which might affect it) that the kidneys are failing

The Interpreter of Investigations Investigations may be divided into those which can be interpreted by the clinician and those which can be satisfactorily interpreted only by the expert In the former category are X rays of fractures and biochemical and haematological figures such as the level of blood urea sugar or haemoglobin in the latter is histology There is no clear line separating these categories The clinician may refrain from interpreting all investigations but expects a report which does this for him He merely studies the report of a chest X ray which says shadow in the right upper zone suggesting pneumonia or he reads that the patient has anaemia treat with iron On the other hand he may study sections of tissue and draw his own conclusions

But to leave the interpretation exclusively in the hands of the radiologist or pathologist is as a rule deplorable However learned and balanced they are they can rarely draw sound conclusions from a particular investigation It should be interpreted in association with the other findings and only the clinician can do this This does not mean that the expert should not offer his opinion On the contrary he should do so and his views will often be of great value but they should not be taken as infallible In difficult cases discussion between the clinician and his expert adviser is the best course

Sometimes the histological appearances are so supremely important that the clinician must depend largely on the expert Moreover the pathologist s opinion here is often accepted as the final court of

appeal and if he is mistaken his mistake may never be discovered If he wrongly concludes that a stomach removed by the surgeon is affected by carcinoma when in fact the lesion is a simple ulcer the effect of his error is to give the surgeon the mistaken belief that he has cured a case of cancer Alternatively only after the lapse of years may an error be suspected The histological finding of carcinoma of the prostate will lead to prolonged treatment by stilboestrol Years later when the patient is still in excellent health (apart from his swollen breasts atrophy of hair and impotence) it may be first suspected that perhaps he never had carcinoma of the prostate

In these circumstances therefore a heavy responsibility rests upon the pathologist The clinician should play his part by not expecting a *confident statement about histology in every case* What he can reasonably ask of the pathologist is that when an unequivocal report is given its reliability can be depended on absolutely

This raises the difficult problem as to how much information the pathologist should have when studying sections There can be no doubt that he should know the exact source of the specimen but whether further details help him to reach a balanced opinion is debatable If the clinician stresses that all the findings point to say Hodgkin s disease the pathologist is encouraged in difficult cases to confirm this opinion If he knew nothing more about a section than that it was derived from a lymph gland his view that the patient had Hodgkin s disease would carry more weight Perhaps the best solution is to compromise the pathologist first studies the section while knowing only its source and then studies it again while knowing every clinical detail If this *makes him change his opinion* he should be wary of giving any but an equivocal report

CHAPTER 4

Principles of Treatment

JOHN W TODD

ASSESSING THE VALUE OF TREATMENT

THE only reliable test of a remedy is the empirical test, giving the word empirical its dictionary meaning of "Based, acting on observation and experiment, not on theory". This view, with certain reservations which will be discussed later, is now widely accepted. Indeed it may seem to be a self-evident truth. But in the past the use of remedies depended not on evidence that they worked—and only a tiny proportion did work—but on tradition, authority and *a priori* speculation in varying proportions; the same is true in many circumstances to-day.

The ultimate basis of a high proportion of the remedies of the past was *a priori* speculation. The individual doctor in 1840 relieved his patients of their pints of blood because it was the universal custom of the time, but behind the custom was the theory that a fevered man's blood contained phlegm, and therefore he should obviously be bled to get rid of this objectionable substance. Behind the widespread practice of starving patients lay the theory that fever is analogous to a fire. To dampen down a fire it is deprived of fuel, therefore to dampen down a fever the patient is deprived of food. The theoretical basis to purging was that there are noxious substances in the bowel of which the body should obviously be rid.

In the very recent past the man who had suffered severe injuries and was found to be in a state of secondary shock, with cold extremities, a subnormal temperature and a feeble thready pulse, was heated by hot water bottles or hot air cradles and given copious drinks of hot sweet tea. Thereby it was clear that the shock would be overcome. Similarly, the cold foot of the man with impending arteriosclerotic gangrene was naturally kept warm by cotton wool and hot water bottles. The youth who was momentarily concussed during a game of football would be kept quietly in bed in hospital for 3 weeks. In this way his brain would be rested and such complications of head injury as persistent headache and irritability would be prevented. The patient who developed anuria would be given massive intravenous infusions containing sodium sulphate because the sulphate ion is not reabsorbed by the kidney tubules and must obviously take with it the necessary large volume of water to maintain it in solution. The patient who had had an abdominal operation was kept in bed for several weeks because to do anything else seemed clearly ridiculous. If he was so "ignorant" as to ask to get up, the grave dangers of doing anything so absurd would be pointed out to him. If the operation had been done for peritonitis he would be put in Fowler's position with a bolster under his thighs and a high back rest to keep his trunk nearly upright. In this way the effusions would fall into the pelvis and, because the pelvic peritoneum has less stomata and absorptive power than the peritoneum underlying the diaphragm, the damage would be minimized.

All these remedies are now dead or dying. The reason for their development is to be found in *a priori* speculation; the main reason for their dying has been the discovery of evidence that they are ineffective or harmful.

A large number of remedies still depend wholly or partly on *a priori* speculation. The peptic ulcer subject is forbidden roughage not because this has been shown to harm him but because it is hypothesized that roughage will irritate the ulcer and prevent it from healing. A similar restriction is put upon the patient with ulcerative colitis for similar reasons. The feverish patient is ordered to drink far more than he desires so as to flush waste products out of the system. If the fever is prolonged he is ordered a very high calorie diet to maintain his strength. The oedematous subject is only allowed a small intake of fluid in order to lesson the oedema. The victim of myocardial infarction is kept in bed for 6 or more weeks because if he gets up earlier the scar on his myocardium will not have healed properly and he will be in danger of getting a ruptured heart or a cardiac aneurysm. The child with rheumatic fever is kept in bed for weeks after his joints have become painless and his fever has gone so that the damage to his heart may be prevented or minimized. The patient with infective hepatitis is given a fat-free diet because this condition is

associated with imperfect absorption of fat and fat will therefore harm him He is also given a high protein diet because animal experiments have shown that protein protects the liver when certain poisons act on it (In the recent past he would have been given a low protein diet because it was hypo thesized that the liver should be rested by diminishing the flow of the products of protein digestion in the portal vein)

It is not suggested that all the remedies just men tioned are in fact useless in the circumstances described many of them may well be valuable No doubt the patient with prolonged fever may do better if he eats more than he desires and the victim of a cardiac infarct who walks about as soon as he feels so inclined may be taking risks But the basis to these remedies is not observation and experiment but theory and until the evidence of observation and experiment has been obtained their value is unproven If the *a priori* speculation of only a few years ago led to Fowler s position prolonged bed rest after operations and the vigorous heating of shocked patients the *a priori* speculation of to day should not be held sacrosanct

When assessing the value of a remedy this impor tant preliminary question should then be asked Is there any evidence to support the remedy or does it wholly rest on *a priori* speculation? This question may be difficult to answer at times but frequently the evidence is either overwhelmingly strong or so meagre as to be of doubtful signifi cance The value of most surgical operations except tonsillectomy and circumcision in infants and of the new anti bacterial and replacement specific drugs has been established beyond question It is the gen eral measures of a vague character such as rest modification in the diet physiotherapy and changes of climate whose value is attested by no sound evidence and which form the happy hunting ground for the theorist To a less extent the same is true of some of the older drugs and mixtures such as the expectorants and the stimulants

Scientific Basis of Remedies When a remedy has been shown by observation and experiment to be valuable all would agree that its use rests on a scientific basis But the phrase scientific basis is commonly used with a different meaning—namely that there is an explanation of why the remedy should work The true basis for our belief in the value of penicillin is that it cures sick people the scientific basis is that when a solution of penicillin is added to cultures of various organisms in the laboratory the organisms die The true basis for the belief that hypotensive drugs are beneficial should be derived by observations showing that they keep patients better over the course of time the scientific basis is that they have lowering effect on the sphygmomanometer readings The true basis for the belief in the value of vitamin B_{12} is that it cures pernicious anaemia the scientific basis is that it is not absorbed by the subjects of pernicious anaemia (owing to the absence of an intrinsic factor present in normal people) and therefore has to be given to them by injection

A remedy with no scientific basis in this second sense of an explanation of how it works is often condemned as merely empirical Indeed in cur rent medical writing it is habitually said or implied that science and empiricism are antitheses We hear much of the so called absurd empiricisms of the past or of the empirical nonsense of the fantastic hell brews of concoctions of urine faeces and snails which our unfortunate ancestors were forced to swallow or of the magical rites to exorcize disease in which they took part But to call this empiricism is ridiculous it is not empiricism but theory gone mad

All this is not to imply that we should make no attempt to understand why remedies are effective or that we should discover new remedies by no other means than trying out new compounds chosen quite blindly on patients On the contrary antibiotics say are discovered by observing the effect of new compounds on bacterial cultures in the laboratory When an apparently effective substance is found it is given to laboratory animals infected by the same organism and the effect is noted by comparison with the course of events in non treated animals Hormone preparations are discovered by giving newly synthesized compounds to animals who have had some endocrine organ removed and noting whether the animals are restored to normal. New drugs which lower the blood pressure are found by similar animal experiments But this in no way modifies the proposition that the final proof of the value of a remedy and the only proof which should be accepted without question is that it benefits sick people

Experience

One kind of experience is that derived from taking part in the study of large scale controlled series by some new drug as is often done under the aegis of the Medical Research Council it will be considered below (p 22) In ordinary language experience is something very different A physician is said to be experienced in a general way because he has been practising medicine for a long time A physician is said to have great experience of a certain disease because large numbers of patients affected by this disease have been under his care irrespective of the manner in which he studied and treated them Ex

perience indeed is a quantitative not a qualitative measure

In the past great weight was put upon this ordinary kind of experience Consid-rable weight is put upon it now though perhaps more by the laity than by the medical profession But that men have made grossly wrong deductions from their own experiences is abundantly clear If a physician of the last century had been asked why he bled starved and purged he would surely have answered that his experience had proved the value of these remedies We can see that his patients recovered in spite of not because of their treatment and that the reason behind it was not practice but theory If the doctors in the past could reach such wrong conclusions from their experience there is no reason to suppose that we must necessarily do better Indeed the greatest caution should be exercised in drawing deductions about treatment from everyday experience Patients differ infinitely many disorders do the same similar cases of most conditions are not often seen by the same doctor memory unless reinforced by careful notes can be highly selective and play false tricks when comparing a current case with a case of years ago and a high proportion of disorders get better as the result of a natural process irrespective of treatment It is very easy to fall into the *post hoc ergo propter hoc* fallacy and deduce that a remedy has been responsible for recovery simply because recovery has taken place

From ordinary experience conclusions may nevertheless be reached about the value of treatment for conditions with an unvarying natural history Experience can demonstrate that operation can cure herniae or hare lips since these conditions never disappear spontaneously This is of little value to the individual doctor since before he starts in practice he already knows that these remedies are certainly beneficial He wants information about less clear-cut matters of which the books speak with differing voices and here it is most unlikely that he will be able to make valuable deductions from his own experience

But exp rience still has some contributions to make The general practitioner may read that the correct treatment for patients with peptic ulcer is the use of numerous vigorous measures when the condition is early (so as to ensure complete healing) including a 4 to 6 week spell in bed a milk and mince diet and the eradication of septic foci His experience may lead to legitimate doubts about these remedies but it can hardly prove that they are valueless However the strong objections to some of these remedies may be brought home to him The spell of weeks in bed will cause many patients to lose money and a few to lose their jobs If he has a peptic ulcer himself the deadly monotony of the official diet may come as a striking revelation Similarly he may become aware that certain operations such as the removal of the chronic appendix or the tonsils may fail to relieve the patient s symptoms Indeed the ordinary experience of practice can probably give more valuable information about the harm which treatment can cause than about its benefits though it cannot give a correct forecast of the likelihood of harm in any particular case

Means of Obtaining Evidence about the Value of Remedies

As just noted ordinary experience can yield information about treatment for diseases with an unvarying course such as hare lips herniae and lipomas Moreover observations on a single person with one of these conditions can prove that for him operation has been beneficial irrespective of any general conclusions The patient whose hernia has disappeared after his operation has not been the less cured by reason of another patient being less fortunate Similar considerations apply to certain medical conditions which can be relieved indefinitely by the continuous taking of drugs The severe juvenile diabetic never recovers if untreated and within a year or two he invariably dies His insulin injections are without doubt responsible for his ability to live a normal life The myxoedematous subject is benefited with equal certainty by his daily dose of thyroid extract

Progressive Diseases

Malignant disease nearly always progresses (though there are occasional exceptions to this rule) but the rate of progress varies greatly One woman with a carcinoma of the breast will be dead of secondary deposits within a few months even though her primary growth has been extirpated within a week or two of the first appearance of a lump A second will have no treatment but will die 15 years later from an unrelated condition her growth having advanced only very slowly throughout One chronic bronchitic will rapidly become worse and die in a year or two a second will hardly change in the course of years Remedies for patients with such conditions as these are more difficult to assess Nevertheless by observing a single patient with malignant disease for many years it may be apparent that an operation has benefited him

because there is then no sign of recurrence There is a possibility of error here the diagnosis may have been wrong When the condition is advanced at the time of operation and particularly when there are secondary deposits there is little risk of error but in these circumstances the patient rarely remains free of recurrence for long Difficulties arise with the very early lesion when the diagnosis of malignant disease depends almost wholly on the pathologist the patients with such lesions are those most often cured of their disease

Acute Diseases

The subjects of chicken pox mumps, a boil the common cold acute tonsillitis and a host of other conditions almost always recover quite quickly Here it is easy to fall into the *post hoc ergo propter hoc* fallacy and to deduce that a remedy given for one of these conditions has been responsible for recovery when in truth this was a natural develop ment This no doubt explains why the various remedies of the past persisted Convinced that the remedy would work the doctor was able to demon strate its effectiveness by the patient s recovery

If a remedy has a sufficiently dramatic effect on those ill with severe potentially fatal or more pro longed conditions this may be apparent with but the briefest observation even though their natural course varies greatly The subjects of meningococcal meningitis gonorrhoea and malaria usually im prove so rapidly with sulphonamide penicillin or quinine that ordinary observations at the bedside can leave no doubt of the value of these drugs

A few acute diseases may be followed by chronic sequelae often after a lapse of years during which the patient remains apparently well Examples are acute nephritis which may be followed by fatal chronic nephritis and rheumatic fever which may be followed by rheumatic heart disease Here the objects of treatment are twofold first to relieve the acute process and second to prevent the sequelae Assessing the value of treatment having the first object provides the same problem as that given by other acute diseases But there are formidable diffi culties in assessing the value of treatment whose object is to prevent sequelae Clearly no useful con clusions can be drawn without a very long period of study Ordinary observation by a single in dividual who sees only an occasional case of one of these conditions is quite insufficient. The only means of solving the problem is a large scale controlled series half of whom are given some remedy and half of whom are not with a prolonged follow up These considerations have not prevented confident statements being made without the support of any such tedious study Thus it has been frequently asserted that if patients with rheumatic fever are rested for months after the acute phase of their disease has passed they will be given the best chance of escaping subsequent rheumatic heart disease

Chronic Relapsing Diseases

Many chronic diseases run a most variable course with relapses and remissions of greatly differing lengths One subject of duodenal ulcer will have only occasional pain separated by long intervals of freedom another will have pain most of the time and suffer various disasters such as haemorrhage and perforation One subject of disseminated sclerosis will have a brief episode of trouble and then remain well for many years before the next episode begins another will have no remissions and be dead within a year Similar considerations apply to rheumatoid arthritis ulcerative colitis asthma chronic arterial disease and many other conditions When treatment is given to provide immediate symptomatic relief—as with alkali for duodenal ulcer or adrenaline for asthma—sound conclusions are easily reached But when the object of treatment is the prevention of relapses the difficulties of assess ment are great indeed Ordinary clinical observa tions are again inadequate and the problem can be solved only by very long term carefully controlled studies Yet confident statements largely derived from *a priori* speculation are often made In the treatment of duodenal ulcer it has been dogmatically stated that many remedies given simultaneously in cluding rest a change in the habits of life or occupation a special diet the avoidance of anxiety tobacco and alcohol the eradication of septic foci and a variety of drugs are essential in preventing relapses

Controlled Series

The real difficulties in assessing the value of treatment are then provided by the subjects of acute recoverable conditions and chronic relapsing diseases with a variable natural history As already suggested large scale controlled series are here of great value When such series are concerned with a drug when half the patients are given this drug and the other half dummy tablets identical in appearance with the tablets containing the drug and when the patients for each kind of tablet are chosen at random (but neither they nor their im mediate medical advisers know what they are having) the results usually provide evidence which cannot be disputed Series of this kind are not only of intrinsic value they also help to mould the climate of opinion by encouraging the view that the only sound test of a remedy is the empirical test

But for the following reasons controlled series are often impracticable

1 To withhold a remedy when patients are likely to be harmed is unjustifiable Indeed controlled series when some of the patients are given nothing except dummy tablets can rarely be made in studying potentially fatal diseases their chief practical use is in studying minor disorders such as tonsillitis or the common cold On the other hand controlled series are quite proper in comparing the merits of two drugs (or two combinations of drugs) in treating serious diseases so long as there is reasonable doubt as to which of the two is the more valuable

2 When the remedy is anything but a drug the effect of suggestion which can have a profound influence (especially when the criteria of assessment are the symptoms) can hardly be eliminated Even pain due to organic lesion can sometimes be relieved entirely by the injection of water Surgical operations physiotherapeutic procedures and manipulation by an osteopath (with all the accompanying mumbo jumbo) have a great suggestive effect on many people However futile these procedures are in the long run they can certainly make people feel better for a time

3 Such remedies as rest diet and physiotherapy are not precisely measurable Often there can be no certainty that patients have had the planned amount of one of them the man ordered to remain in bed and eat a restricted diet may do neither yet fail to confess his sins to his medical adviser Many general measures are ordered for very long periods even for the remainder of the patient s life The subject of peptic ulcer is often told to refrain for ever from eating fried foods pickles sauces and skins the victim of a cardiac infarct may be ordered to be a semi invalid for the rest of his days and the consumptive who has apparently recovered completely may be told that he should always go to bed early sleep with the windows open and eat plenty of rich fatty food Even if difficulties of these kinds were overcome and a controlled study of one of these general measures demonstrated its value the problem would still remain of deciding which particular feature of it was responsible for the beneficial effect If the subjects of peptic ulcer who take a special diet are shown to progress better than those who do not, it will still be necessary to inquire whether the important factor is the frequency or the nature of the food if the latter what are the particularly valuable qualities of the food if the former whether frequent food is any better than frequent alkali

Perhaps the main explanation for the lack of controlled studies of the general remedies is the absence until very recently of widespread doubt as to their value The great physicians of the nineteenth century performed a service to medicine by their therapeutic nihilism towards the drugs of the time only in the last few years has there been much questioning of the traditional views about these general measures The onus of proving the value of drugs especially new drugs is rightly put upon their advocates but the onus of proving the value of régime rest diet and other general remedies is put upon their opponents they continue to be used until proved valueless or harmful.

Anyone who overcomes these formidable difficulties which hinder controlled studies of the general measures does a great service to medicine in shedding light into a very dark corner Useless drugs rarely do appreciable harm but useless régime diet and physiotherapy are far from benign The man who is needlessly kept in bed for only a few weeks has to endure the tedium of this period may suffer financially may worry about himself and may develop such complications as venous thrombosis If these general measures are wrongly advised for a long period or a life time they can cause far reaching and disastrous effects by unnecessarily turning people into invalids and encouraging hypochondriacal traits But valuable as controlled studies would be perhaps more valuable would be a change in the climate of opinion If it were more widely realized that *a priori* speculation is never a complete recommendation for a remedy and that most general measures in most circumstances are based on nothing better the application of many remedies would surely die a natural death without involving anyone in the tedium of elaborate controlled trials

Uncontrolled Studies

When dealing with diseases of little varying natural history remedies can be compared from the effect of each on this known natural course Assessing treatment for malignant disease is usually done in this way patients being followed for some 5 or preferably 10 years The proportion of patients then alive and free of recurrence gives some indication of the treatment s efficacy But the natural history of malignant disease varies a good deal and the results of series of this kind are apt to give a more favourable impression than the reality because some cases of malignant disease advance very slowly Even when dealing with acute recoverable conditions and chronic relapsing conditions of infinitely variable natural history (about which so many misconceptions have arisen) large scale uncontrolled series may be of some value A series of 100 cases of pneumonia treated by a new drug without a single death would certainly suggest that the drug is effective in spite of the infinite variety of pneumonia and its greatly varying diagnostic criteria

THE INDIVIDUAL PROBLEM

General knowledge of a remedy is sometimes directly applicable to the particular patient without much consideration of his special circumstances If typhoid fever is diagnosed the latest information is studied and chloramphenicol is seen to be the drug of choice This drug is then prescribed in the recommended dosage But even when the patient has some condition for which there is a remedy of undoubted value there are often factors which oppose the use of this remedy in the particular case These factors include the age the intelligence and personality and the presence of some other bodily disease

Age The age alone should rarely influence medical treatment of certain value Pernicious anaemia iron deficiency anaemia or pneumonia should be treated however old the subject But with conditions amenable to surgery age should often make a great deal of difference In general innocent surgical lesions in very old people should be left alone unless they are causing marked discomfort since the general upset of an operation is apt to be very disturbing to them while the benefits from it are likely to be small Malignant conditions too can often rightly be left alone in the very old The carcinoma of the breast in an aged woman which is causing no immediate trouble will probably advance extremely slowly and she may die of an unrelated condition

Psychological State The intelligence and personality should hardly modify the treatment given to those with acute diseases or with such grave disorders as malignant disease or tuberculosis But they should often make a great deal of difference in treating chronic innocent conditions The success of orthopaedic operations for such conditions as torn semilunar cartilage of the knee hallux valgus and pes cavus greatly depends on the active co operation of the patient in carrying out remedial exercises and in other ways They should therefore be performed only reluctantly on the stupid or the hysterical In treating diabetes mellitus a complicated diet sheet and a mixture of insulins (with instructions as to how the dose of each should be modified) may be suitable for the intelligent man but unsuitable for the illiterate dullard In advanced senile dementia where the patient is bedridden incontinent and unable to feed himself it is doubtful whether active treatment should ever be given If such a person develops a strangulated hernia or pneumonia to prolong his life by operation or by penicillin is hardly a kindness either to him or his relatives This situation involves religious and moral considerations Some might argue that the doctor s duty is to prolong life in all circumstances I do not share this view

Complicating Diseases The presence of a second disease should often profoundly influence the treatment given for the disease under consideration The advanced chronic bronchitic is an unsuitable subject for surgery If he has a chronic gastric ulcer gastrectomy may be most successful if he survives but the additional hazards of operation for him are such that only severe symptoms unrelieved by medical treatment would justify it If a man with inoperable malignant disease develops diabetes this should be treated far less seriously than is diabetes in an otherwise normal person If he has few or no diabetic symptoms the matter is best ignored if he has severe thirst and polyuria no doubt he should be given insulin but there could be no question of stabilizing him on a precise diet and insulin intake Obesity should greatly influence the treatment given for benign surgical conditions Operations for herniae deranged knees or osteoarthritic hips in the grossly obese involve considerable risk and are often unsuccessful

RADICAL AND SYMPTOMATIC TREATMENT

The main objects of treatment are in the final analysis to save or prolong life and to remove or prevent symptoms Saving and prolonging life are as a rule achieved by such specific measures as anti bacterial drugs hormone preparations radio therapy and some varieties of surgery To withhold measures of this kind when applicable and to give instead symptomatic remedies is in general a serious error There are nevertheless exceptions to this rule As was just noted above the subject of advanced senile dementia who develops a strangulated hernia or pneumonia should be given the symptomatic not the radical treatment

When dealing with patients who have some comparatively innocent condition the situation is often very different Even here if the condition is certainly responsible for the symptoms and if the radical treatment is almost free of risk and will in high probability get rid of the condition it should usually be given But innumerable people have some benign abnormality which bears little or no responsibility for their symptoms in dealing with them to concentrate upon radical treatment may be a great mistake *This mistake is made frequently* If people with blood pressure readings above average have such symptoms as transient giddiness or occa

sional headache or even when they have no symptoms and their elevated blood pressure is discovered by accident, they may for ever after have treatment designed to lower the sphygmomanometer readings This can hardly fail to cause forebodings to the patients and if they are introspective and nervous they may become obsessed with their blood pressures. Numerous children who are able to take part in all activities are found on routine examination to have "flat feet" or curvature of the spine In consequence they may miss school while attending classes in which they do exercises designed to correct these errors and their parents will naturally be worried Recruits to the Armed Services may be scrutinized carefully and have operations for small bulges in their groins which are causing no trouble Not so long ago they would have operations for varicocele a recogniz d indication for this operation being that the subject hoped to join th• Army There is indeed a tendency to assume that anything which can be called an abnormality should be corrected " and too little consideration is often given to the question whether this is causing or is likely to cause trouble

Treatment given to people with abnormalities who are free of symptoms can be defended only on the ground that they will later be prevented from developing symptoms Thus it may be argued that by treating elevated blood pressure subsequent incapacitating headaches or strokes may be prevented or that by treating curvature of the spine by exercises subsequent backache may be prevented The only evidence on this matter of any value would be large scale controlled series lasting for very many years There is no such evidence and *in its absence there is no justification for assuming* that the alleged benefits of the treatment will occur The onus of proof should rest upon those who advocate the treatment not upon those who doubt its value

Even when there is no doubt that some lesion is responsible for the symptoms the radical treatment is not always the best. Many patients with osteoarthritis of the hip can be kept fairly free of pain by regular aspirin (and pain is usually their main complaint) This simple symptomatic remedy should often be preferred to the radical treatment of excising the head of the femur and the acetabulum and replacing them by stainless steel or plastic substitutes Most patients with sciatica recover more or less completely It is better to keep them going with symptomatic drugs or perhaps to advise a spell in bed or some d⌄vice to immobilize the spine rather than resort to the radical procedure of removing the prolapsed disc which is causing their pain Patients with duodenal ulcer can often b⌄ kept well merely by taking massive quantities of alkali this has advantages over the radical treatment of gastrectomy which is not devoid of risk and is sometimes followed by troublesome sequelae

LIFE-PROLONGING MEASURES FOR THE DYING

Many conditions although invariably fatal are susceptible to treatment which will prolong life Patients with irremovable carcinoma of the bowel may have short-circuit operations Widespread secondary deposits may be treated by radiotherapy by stilboestrol or testosterone or by adrenalectomy The *victims of leukaemia may be given radio*therapy steroids or blood transfusions Malignant hypertension can be treated by methonium compounds or a rigidly salt free diet and chronic nephritis with nitrogen retention and anaemia by blood transfusions and intravenous fluid

Patients with conditions of this kind provide a common and distressing problem Should every step be taken to keep them alive as long as possible or should they be given merely symptomatic treatm nt and be allowed to die in peace? No easy answer can be given to these questions and each cas• must be decided on its m rits

In practice there is a tendency to give the life prolonging measures in most circumstances A surgeon may find it difficult *merely to open an* abdomen and shut it again and may do a short circuit operation when there is no reasonable hope even of relieving the symptoms for long Many radiotherapists seem unwilling to admit that radiotherapy would be futile in the case under consideration Some physicians are unwilling to stop the *repeated blood transfusions which are keeping the* victim of acute leukaemia alive This attitude is understandable but there are surely many cases in which the right and kind course is to give the patient analgesics and hypnotics make him as comfortable as possible and let him die

In this difficult situation it may be felt that the right person to make the decision should be the patient himself His life is in the balance cannot he say whether he wishes it prolonged? But if he is to make the decision he must be supplied with all the facts This means that he is told (1) he has a fatal disease (2) if nothing is done h• will probably live a specified time and suffer certain symptoms (3) if he has some treatment he will suffer a good deal of discomfort *from this may then be*

better temporarily and perhaps be able to return to work but after a few months will relapse and die just as uncomfortably as if he had never had the treatment All our instincts rebel against such behaviour Even if a patient is an intelligent man who asks to be told the truth in practice no one would do this and this would be equally true if he were a medical man himself

Should then the opinion of the relatives be sought? They should be told the facts and in particular *it must be made clear that there is no hope* of cure but only of temporary improvement If they urge that something be done or alternatively if they offer the opinion that the kindest course is to leave well alone no doubt their views should be taken into consideration But to insist that they alone reach the decision is wrong How could the parents of a child dying of malignant disease possibly take a balanced view? The more common situation when the relatives are mature adults and the patient is an old parent is much less distressing but even here it is asking too much to leave the decision to them alone If they oppose active steps they may feel conscience stricken after the patient is dead aware that he might still be alive If they decide in favour of treatment they may also feel conscience stricken when after temporary improvement he develops distressing symptoms And the relatives may be unable to agree among themselves

The doctor then must reach the decision perhaps with the help of a second opinion He should then tell the relatives which course he advocates and give them the reasons for his view As a rule they will probably accept what he says without question In assessing the situation many factors should be borne in mind such as the patient s age circumstances and temperament the ill effects of the treatment the likelihood of relief of distressing symptoms and the likelihood of a prolonged remission *or prolonged relief*

In general the farther removed in age the patient is from the prime of life the less should he be treated To give radio therapy to a man of 90 with secondary deposits seems in general misguided To give *blood transfusions and* other treatment to a 2 year old infant with acute leukaemia is perhaps even more misguided When an infant dies so quickly from leukaemia that there is no opportunity for taking action few medical men would dispute *that this result is fortunate* Prolonging the infant s life therefore gives him very little but gives his parents an agonizing period which they will probably never forget On the other hand when the patient is the mother of a young family it seems the *right policy to prolong her* life as far as possible provided she can be kept fairly active Whether this is the kindest course from her angle is debatable but there is little doubt that it is so from the family s

Treatment should more readily be given to the patient with relatives who are fond of him and will willingly look after him *than to the one who is* alone in the world But his temperament is perhaps more important than his circumstances The extravert of genial personality may apparently be almost oblivious of his state and live quite happily almost *until he dies whereas the depressed introvert may* be continually conscious of his unfortunate condition

An important reason for giving life prolonging treatment is that this will also relieve severe symptoms which will not necessarily recur The value of radiotherapy in treating patients with bronchial carcinoma is in most cases doubtful but if there is distressing stridor there is a good chance that this will be relieved and will not return the patient dying in a less unhappy state Radiotherapy may also be effective in relieving the pain of osseous secondary deposits and this too will not always recur (When pain is the main symptom cordotomy or leucotomy may alternatively be used which are not also life prolonging and these may be preferable)

A second reason for giving treatment is that there is a good chance of causing marked and prolonged retrogression of the process or even complete remission The subject of prostatic carcinoma with osseous secondary deposits may sometimes respond so excellently to stilboestrol that he remains well for several years and may even die of an unrelated condition A confident prophecy as to the extent and persistence of retrogression cannot unfortunately be made Even an occasional patient with say cerebral glioma or bronchial carcinoma (in the absence of obstructive symptoms) will improve remarkably *after radiotherapy although the great* majority with these conditions respond hardly at all No doubt this is one reason why the most unpromising subjects are sometimes treated the doctor will be able to remember a similar case years ago who apparently responded to an astonishing degree

A general reason sometimes advanced for giving life prolonging treatment to hopeless cases is that only by treating such people will more effective agents be discovered This no doubt justifies the trial of new remedies but it does not justify the use of remedies which have already been tried on a large scale and found wanting A great number of remedies have been tried for acute leukaemia all of which are sometimes beneficial but none of which have ever kept a patient alive for longer than a year or two Persisting with these particular remedies

is most unlikely to help in the discovery of new and more effective ones

A final reason for giving this treatment is the possibility of diagnostic error Patients who have been given up as hopeless on account of "secondary deposits" in the peritoneum occasionally recover because in fact they have tuberculous peritonitis But such life prolonging remedies as the hormones or radiotherapy would have no beneficial effect on non malignant conditions and the possibility of diagnostic error does not justify them On the other hand the surgeon who is contemplating a short-circuit operation for what seems to be malig nant bowel obstruction should be more inclined to do this operation if there is any chance that the process is benign When a patient is severely anaemic from bone marrow depression there is sometimes difficulty in differentiating between aplasia of the marrow and leukaemia Whatever view is taken of treating leukaemia by transfusion until time has put the matter b~yond doubt such a patient should be transfused

CHAPTER 5

Means of Treatment

JOHN W TODD

REST

THERE is very little evidence about the value of rest in most circumstances Pronouncements about this matter made in books persist for many years with no more to recommend them than custom ultimately they are based *on a priori* speculation

In spite of this unsatisfactory state of affairs there is sometimes a compelling ground why a patient should rest—namely that he is incapable of doing anything else The victim of a stroke paraplegia or an epileptic fit has no choice but to rest Those with many other acute illnesses may sometimes be capable of dragging themselves about but their natural inclination is to stay in bed

The practical questions to be asked then are Does the patient s natural inclination indicate how long he should rest? Under what circumstances should rest be advised although the patient is anxious to get up? and Under what circumstances should the patient who is anxious to rest be urged to get up? Because of the paucity of evidence such questions can be answered only tentatively

It seems reasonable to make the preliminary assumption that less or more rest than that indicated by the natural inclinations should be advised only when there are positive grounds for doing so The situation is complicated by the fact that people s apparently natural inclinations are often in fact not natural but acquired The man who has a mild febrile illness may stay in bed not so much because of his feelings as of his belief that if he gets up his recovery will be delayed

In most acute illnesses and after most surgical operations good grounds for departing from the assumption that the patient s natural inclinations are the best guide are rarely seen Yet until recently this assumption was hardly ever made Those who had any serious operation were automatically kept in bed for weeks The situation has now changed so greatly that many surgical patients are forced out of bed almost as soon as they have recovered from the anaesthetic and urged to walk about The basis of this practice is that the incidence of such complications as thrombo-embolism and lung collapse will be diminished and there is no evidence that it is harmful in other ways (though it may sometimes be unpleasant) and it undoubtedly hastens recovery Complications of this kind follow acute medical illnesses too so there are grounds for advocating early ambulation or at least leg exercises in bed for those who have such illnesses

The patient who remains completely in bed must use a bed pan There has recently been a widespread revolt against the bed pan and it has been pointed out that using it as well as being unpleasant involves the expenditure of much energy Physicians who advocate rest should therefore insist on commodes rather than bed pans Provided that a patient is not anchored to the bed by orthopaedic appliances and is in possession of his faculties there is rarely justification for using the bed pan for defaecation In hospital wards it can satisfactorily be replaced by a wheeled chair made like a W C seat on which the patient can be taken to a closet outside

For many chronic conditions rest of a degree much greater than that which the patient is naturally inclined to take is often advised for very long periods or even for life The subject of a cardiac infarct who has made a complete recovery may be told that he should always live quietly must never run for buses or trains and should rest for an hour after meals with his feet up Those with rheumatic heart disease or elevated blood pressures may be given similar advice and those who have had pulmonary tuberculosis may also be told that they should always spend some ten hours every night in bed

The only means of testing advice of this kind would be a large scale controlled series of patients over many years Whether or not it is beneficial in prolonging life or preventing relapses in some cases it undoubtedly harms the patient mentally If he takes the advice seriously he must be given the impression that he is an invalid If he is introspective he will be liable to worry about his heart or blood pressure and develop somatic symptoms of anxiety In turn he may ascribe these symptoms to his disease and thus be given a further source of worry Before restriction of activity is advised these

things should be remembered and if it is still advised the patient should be told that palpitation exhaustion and other symptoms are caused by worry not by bodily disease

Even if it is in fact true that those with elevated blood pressure cardiac lesions and other conditions will benefit by living a semi invalid life to the extent of increasing their life s span from say 12 years to 15 years it does not automatically follow that a life of this kind should be advocated The patient may prefer to run the risk of shortening his life Who would blame him? Is not a short and happy life better than a miserable and long one? When the active man s end comes he may die in harness rather than in bed—an achievement for which most men would envy him

DIET

The same assumption should be made about diet as about rest i e the patient s natural inclinations should determine his diet unless there are positive grounds for the contrary Such grounds are rare in most acute illnesses and their victims can be encouraged to eat what they like Few of the traditional restrictions and recommendations such as forbidding solids to those with fever forbidding red meat and insisting on milk and so called bland dishes are based on evidence

In certain prolonged illnesses such as enteric fever and pulmonary tuberculosis there are theoretical grounds for urging the patient to eat more than he desires particularly of protein Such diseases cause much loss of weight and it can be argued that overfeeding will minimize or prevent this and maintain the patient in better shape to combat his illness Even here there is no evidence from controlled series Those whose tuberculosis is advancing are usually wasted and those whose tuberculosis is retrogressing are not it is true but this does not prove that tuberculosis can be made to retrogress by extra food When tuberculosis is successfully combated by anti bacterial drugs or surgery increased weight comes naturally

If there are grounds for advising a patient to eat more than he is naturally inclined merely to order him a 3 000 calorie diet is not enough The diet may be so unpalatable that most of it remains on his plate Rather should efforts be made to discover which of the high calorie or high protein foods he likes most That one man s meat is another man s poison is perhaps more true of the sick than of the healthy the man who will relish almost anything when well may become very difficult about his food when ill

Among the conditions in whose treatment the patient s natural inclinations do not give correct indications about diet is obesity which can be overcome only by the rejection of the natural impulse to eat several large meals every day The same is true of the common obese type of diabetes arising in middle life

In a few circumstances there are grounds for restricting certain constituents of diet One such restriction is that of wheat and rye gluten in treating coeliac disease which is profoundly beneficial Another is that of sodium in the treatment of most conditions causing oedema although here there are usually alternative methods of treatment which may lessen the degree of sodium restriction required (and a diet almost free of sodium is most unpalatable) Many commonly advised restrictions on the other hand such as roughage-containing foods spices and roast or fried articles in the treatment of peptic ulcer are of unproven value and depend not on evidence but on theory

A few people are allergic to single items of food such as shellfish or strawberries Here the obvious advice is to avoid these items Many people claim that certain foods give them indigestion " They include anything fried roast or greasy twice cooked meat cooked cheese onions spices and fruit skins No doubt this claim is sometimes well based especially in regard to large quantities of cooked fat but the matter is complicated by the widespread public awareness that articles of the kind described are indigestible There is a common tendency to find a cause for symptoms and to the dyspeptic a convincing cause is food He may therefore ascribe his wind nausea or discomfort to some dish which was in fact innocent Similarly the public know that those with peptic ulcer should live on mince and slops and that those with gall bladder disease should avoid fats and eggs If a peptic ulcer subject has a relapse he naturally ascribes this to his failure to keep strictly to bread and milk sieved vegetables and steamed fish There is here a further complication if a man is sufficiently convinced that some dish will upset him it may do so not because of the dish s nature but because of his conviction The psychological aspects of food are indeed often most important Items which are relished by the inhabitants of some countries may be thought repellent by the inhabitants of others Few Englishmen would willingly eat the snails or frog s hind legs which are relished by the French

The patient who claims to be upset by certain foods does not therefore provide a simple problem

with the simple solution that the offending food should be avoided If he believes that only a few unimportant dishes are bad for him there is perhaps little point in pursuing the matter But if he has convinced himself that he can digest only tender *chicken steamed fish lightly* poached eggs black grapes and other expensive dishes an effort should be made to persuade him that his beliefs are mistaken

Patients who are comatose stuporose or delirious provide a special problem for their natural inclinations are of no help in prescribing diet They must be fed artificially and the amount and composition of their food must be decided on theoretical grounds Such people may be fed and watered by the intravenous and rectal routes as well as by mouth Although an adequate water and salt intake can be given rectally or intravenously it is not possible to give an adequate calorie and nitrogenous intake by the rectal route and very difficult to do so by the intravenous route As a rule food and water should be taken through the stomach which is the natural route When the patient is comatose or so stuporose or delirious that he cannot be persuaded to swallow a nasal tube going down his oesophagus is necessary

Patients unable to swallow or with repeated vomiting cannot be fed through the mouth When there is high obstruction a possible solution is gastrostomy or enterostomy Otherwise the intravenous route is usually the best especially when the patient s condition is very bad since large amounts of fluid can be given in this way Intravenous therapy can have a dramatic and often life saving effect on patients who are dehydrated from pyloric stenosis and other causes of vomiting

Fluid Intake When a patient is in full control of his faculties his natural inclinations will as a rule correctly indicate the amount of fluid he should drink just as they indicate his activities and food intake But in the past the natural inclinations were seldom allowed to take charge The oedematous and those who had recently bled from peptic ulcer were traditionally allowed a very small fluid intake —say 2 pints daily in the former case and only a little ice to suck in the latter They consequently suffered greatly from thirst This restriction rested entirely on theory The evidence of recent years shows that the restriction neither lessened the oedema nor stopped the haemorrhage Once more therefore evidence has driven out *a priori* speculation and patients with oedema and haematemesis no longer suffer as they did

The natural inclinations are still often thought to be an unsound guide to fluid intake in treating those with acute febrile illnesses Fluids may be pushed or forced to the point of toleration or some such specified figure as 6 or 8 pints daily may be prescribed This rests on the theory that increasing the urinary output will flush noxious products of the disease out of the system (Just as in the past infections were supposedly eliminated by vicious purges) There is no evidence to support this theory though pushing fluids in contrast to jalap or calomel can hardly do much harm

The natural inclinations are an inadequate guide to fluid intake when there is a disturbance of the body s electrolytes such as sodium chloride deficiency This is often due to excessive vomiting here there are obvious grounds for giving fluid and salts intravenously When salt deficiency is due to excessive sweating the subject may be dehydrated but not thirsty He requires salt as well as water and will often relish a dilute salt solution

PHYSIOTHERAPY

Among the procedures which may be put under this heading are remedial exercises splintage manipulation and traction passive movements massage the application of heat and cold many kinds of electrical treatment heliotherapy and perhaps colonic lavage Some of these procedures are totally different in principle from others and it is hardly possible to make generalizations covering them all

Remedial exercises are of certain value in many circumstances Indeed exercise is a universal antidote to weak and wasted muscles whether general or local though there may be other features of the case making exercise impossible or inadvisable for a time The old person who has been ill in bed and cannot walk unaided must be helped and cajoled until his muscles are strong enough to keep him going alone when he will automatically maintain himself The athlete who has developed weakness and wasting of the quadriceps after injuring his knee must exercise this muscle until it is strong again

The value too of splintage and of manipulation and traction in some circumstances cannot be doubted The pain and disability of a wrist affected by rheumatoid arthritis may be greatly lessened by immobilization in plaster When the plaster is removed after a few weeks the wrist is much less painful and swollen and much of the improvement may be maintained Back splints applied to arthritic knees which are tending to flex are surely effective *in some degree in keeping them straight Traction* applied to the head in some cases of the brachial neuralgia syndrome is followed by such dramatic

relief that this procedure is clearly responsible for the improvement Repeated manipulation is sometimes the manifest cause of the increased range of movement of a joint

There is little evidence of the value of massage heat cold electricity in its many forms and heliotherapy Most of such value as they have is in relieving symptoms they have not been shown to have any effect on the course of more than a very few disease processes

Passive physiotherapy need not be condemned because it has no more than a symptomatic effect If it could relieve the pain of rheumatoid arthritis while leaving the joint swollen and stiff it would be an enormous boon But its symptomatic benefits are usually comparatively slight so the question arises whether the patient derives more relief from say attending a hospital three times a week for an hour s treatment by diathermy than by taking 2 tablets of aspirin every 4 hr No general answer can be given to questions of this kind It is very difficult to give an answer in the individual case since the degree of relief depends on so many variables including the patient s conviction about the respective treatments his mood and the personality of the physiotherapist However treatment by tablets has great advantages over physiotherapy since it is far cheaper simpler and less time-consuming

Physiotherapy is often said to do good by its psychological effect Indeed massage especially when performed by an attractive young woman heliotherapy and many kinds of electrical treatment (as when shocks are given or sparks are seen) have a great psychological effect on many people If they are suggestible and have faith in the treatment they may derive considerable symptomatic relief Sometimes no doubt gross hysterical manifestations can be abolished in this way If by this psychological effect patients could be cured and remained well thereafter there would be every justification for using these dramatic kinds of physiotherapy Benefit of this degree rarely if ever occurs the most that can be claimed is some temporary improvement In the long run the treatment may do more harm than good since the patient when he relapses will demand the same electricity or massage which made him better before He becomes convinced that these elaborate procedures are essential for his health This belief is harmful the belief he should have is that his future depends more on his own efforts than on the activities of others In practice therefore one should be very chary of using physiotherapy for its psychological effect

There is a great public demand for passive physiotherapy Indeed treatment to many of those with the chronic rheumatic diseases means physiotherapy They may admit that aspirin gives relief but they may say nevertheless that they take it only when the pain compels them because it is a drug which dulls the pain but does not cure the disease This desire of the public for physiotherapy is difficult to resist and is responsible for its prescription on an enormous scale although the prescriber is aware that it can do little good When as often happens a patient asks for a course of physiotherapy because of a relapsing condition which he insists was helped by a previous course it is hardly possible to refuse him The situation is similar when a patient claims that physiotherapy is the only thing which keeps him going although he admits that it does not cure him Nevertheless the patient who has relied on his own efforts almost certainly does better in the long run than the patient who has spent many hours reclining while others massage him and give him heat electrical treatment and heliotherapy We ought therefore to discourage passive physiotherapy and make remedial exercises and other kinds of activity the keynote in physiotherapy departments

ANTI BACTERIAL DRUGS

Apart from quinine and mercury nearly all the drugs specific against infections were discovered in this century Until Domagh showed in 1935 that the sulphonamides overcame many infections the chief advances were the treatment of syphilis yaws and trypanosomiasis by arsenicals and kala azar by antimony Following upon the isolation of penicillin in 1941 new discoveries have been made in a great and continuing flood In addition to a vast number of antibiotics para aminosalicylic acid and isonicotinic acid hydrazide have been introduced for tuberculosis and the sulphone compounds for leprosy The situation is so fluid that recommendations about the anti bacterial drugs are liable to become out of date very soon after they have been written

Indications for Anti bacterial Drugs

The surest indication for an anti bacterial drug is that a patient has an infection due to an organism which is certainly susceptible to it Frequently isolating and identifying the organism is impracticable

or involves long delay so the problem constantly arises of deciding whether a drug should be given *although the organism is unknown If there were* a drug which cured many infections but never had ill effects its general use for patients affected by undetermined organisms could rightly be advised As there is no such drug the rights and wrongs of giving drugs before the organism is known can be considered only in the light of the particular circumstances of the case

In general the attempt should be made to isolate the organism when there is a good prospect of success The organism can be found in most cases of urinary infection meningitis malaria enteric fever dysentery pulmonary tuberculosis and infective endocarditis When one of these conditions is suspect the appropriate specimen should therefore be sent to the laboratory before the drug is given If it is given first the subsequent isolation of the organism may be difficult or impossible This matters little when the infection is say tonsillitis but *it matters a great deal when it is infective endo*carditis tuberculosis or enteric fever

Whether or not the drug should be given before the laboratory report is received also depends on circumstances When the patient has meningitis which can be established by the naked eye and microscopical appearance of the cerebro spinal fluid the administration of the drug or drugs most likely to be successful (probably the combination of a sulphonamide and penicillin) should be begun immediately because delay might be fatal When the report on the nature of the organism and its sensitivity *in vitro* has been received a change in the prescription may be indicated When there is a urinary infection whose presence can immediately be confirmed by the pyuria a sulphonamide may rightly be given at once A change in the drug can be made later if this is indicated by the organism cultured and its *in vitro* sensitivity or by the poor clinical response In other circumstances every effort should be made to isolate the organism before the drug is given This is true of infective endocarditis The delay of a few days is unlikely to do harm if the diagnosis has been wrongly made the patient is subjected to an unnecessary course of injections for 6 or so weeks and the precise nature of the organism and its *in vitro* sensitivities are often valuable There is usually no urgency in beginning treatment for pulmonary tuberculosis so a preliminary prolonged search for the organism is justifiable though if the organism is not found but the other features of the case strongly favour this disease the treatment may still rightly be given

On the other hand in many circumstances it is impracticable to find the responsible organism as when there is an inflammatory process in the abdominal cavity but laparotomy is inadvisable When *the findings* suggest acute cholecystitis it is sound policy to give the drug which will deal with the organisms usually found in this condition A similar situation arises when there is a deep inflammatory process affecting a limb When the patient has a chest infection numerous organisms may be found in the sputum and there may be doubt as to which is responsible In fact some of the organisms may have come from the nasopharynx not from the bronchial tree and are unrelated to the illness Alternatively a virus or an organism which has failed to grow in the culture medium is responsible Although culturing the sputum may be worth doing in the light of these difficulties penicillin (which is the drug *most likely to be effective* and *least likely* to do harm) may rightly be given immediately Moreover in the ordinary circumstances of general practice it would be impossible to isolate organisms from the sputum in all cases of chest infection

A particularly difficult situation is provided by the patient with infective illness whose nature is obscure Should he ever be given an anti bacterial drug blindly? This is justifiable if he may have an infection which cannot be excluded quickly but is potentially fatal or liable to cause permanent *ill* effects *if treatment is delayed* An infection fulfilling these criteria is malignant tertian malaria and if this condition is possibly present anti malarial drugs should be given even though the organism cannot be found in the peripheral blood In non malarious countries obscure fever is often due to viruses which are susceptible to no drug and if it is due to a bacterial infection delay is unlikely to do harm Even here if the patient is very ill with a high swinging fever and a marked leucocytosis (which favours a bacterial rather than a viral infection) the blind use of a drug may be proper though a blood culture should usually be taken before it is begun

Sometimes the response to a drug is *itself* a useful diagnostic pointer Practically there are difficulties here because it may be by no means certain that there has been a *favourable* response The wrong conclusion that a drug has been responsible for recovery when in fact the recovery was co incidental is easily reached Only when the improvement is dramatic and follows immediately upon giving the drug is it justifiable to deduce that the one was probably the cause of the other On the other hand an unfavourable response may be obvious and this may make certain infections highly unlikely The persistence of fever after giving anti malarial drugs for example virtually excludes malaria

Abuse of Anti bacterial Drugs

The anti bacterial drugs are perhaps more abused in treating mild infections when the diagnosis is clear than in treating severe but obscure infections In the latter case the defence that to give the drugs is to be on the safe side can sometimes rightly be made in the former case it is difficult to sustain Patients with acute throat infections are often given *penicillin* or a sulphonamide Yet without treatment most throat infections subside spontaneously in a few days It is usually better merely to prescribe an analgesic and leave the rest to Nature than to give one of the drugs with the consequent risk to the patient of toxic effects and the risk to the general population of encouraging the development and spread of resistant strains One defence of giving the drugs here is that the risk of nephritis and acute rheumatism will be lessened But this risk is extremely small except when the patient has previously had an attack of acute rheumatism one of the drugs should then be ordered Similarly it is doubtful whether the drugs should be given for single boils other superficial skin infections and small whitlows They usually clear up quickly and the responsible organism is in most cases the staphylococcus which is particularly likely to develop resistance Indeed because so many staphylococci have already done this the response to the drugs may be poor

A common use of the anti bacterial drugs which probably does more harm than good overall is as a prophylactic after surgical operations If all clean surgical cases are given a course of penicillin to prevent wound infections the wounds may be invaded by resistant organisms perhaps with the most serious consequences Rather should efforts be made to diminish the number of organisms and to minimize the possibility of cross infection by doing dressings in special rooms and other measures

Combinations of Anti bacterial Drugs

On theoretical grounds a combination of drugs may apparently be superior to a single drug in treating patients who have mixed or multiple infections or are obscurely ill by providing a wider anti bacterial spectrum In addition a combination may be synergistic (i e the anti bacterial effect of the combination is greater than that of the sum of each drug acting alone) or may prevent the appearance of resistant strains On the other hand the risk of toxic effects and sensitization reactions may be increased by using more than one drug some organisms may simultaneously develop resistance against two drugs and some drugs may be antagonistic

The effect which drugs have on each other s anti bacterial action is a most complicated and imperfectly understood matter It cannot be assumed that the results of *in vitro* experiments necessarily indicate what will happen *in vivo* or even that animal experiments always reflect what will happen in man The only sound means of comparing the effects of two drugs with one in men is by a carefully controlled experiment on patients Few of such experiments have been p rformed

Mixtures of the bactericidal antibiotics (including penicillin streptomycin bacitracin and neomycin) *in vitro* are often synergistic may be additive but are never antagonistic Mixtures of the primarily bacteriostatic antibiotics (including the tetracyclines chloramphenicol and erythromycin) are additive Mixtures of bactericidal with bacteriostatic drugs may be synergistic additive or antagonistic depending on their relative amounts the organism concerned and other factors The reason for the antagonism between bactericidal and bacteriostatic drugs may be that the bact ricidal drugs chiefly act on the growing phase of the organism so the bacteriostatic drugs by preventing growth interfere with their operation Penicillin and a sulphonamide are thought to be additive

There are very few situations in which synergism has been clearly demonstrated in clinical practice Examples are penicillin and streptomycin for *Strep faecalis* endocarditis streptomycin and a tetracycline for brucellosis and penicillin with chlortetracycline for staphylococcal endocarditis

Only in the treatment of tuberculosis has it been conclusively shown that combinations of drugs will hinder the development of resistant strains These strains seem to result from mutations not from the selective propagation of strains which are already resistant It is thought that if the chance of a resistant mutant developing against each of two drugs given separately is 1 1 000 the chance of a resistant mutant developing against both when given together is 1 1 000 000 A single drug therefore should never be used in treating tuberculosis

The clearest indication for using combinations of drugs in treating mixed or multiple infections is when a patient is affected simultaneously by two independent infections not responsive to the same drug This is very rare in temperate countries but common in the tropics The patient who has malaria and pneumonia should be given both anti malarial and anti pneumonic drugs A much more difficult

situation is provided by infective processes due to a variety of organisms such as peritonitis or lung abscess or other chronic lung infections Although a combination of penicillin and streptomycin has been widely used in both these circumstances with good results it is doubtful whether they are usually superior to a tetracycline alone or in the case of lung abscess to penicillin alone On the other hand the tetracyclines have the objectionable feature of causing alimentary side effects and their widespread use encourages the development of resistant staphylococci They are also very expensive Urinary infections associated with more than one organism may sometimes appear on the basis of *in vitro* sensitivity tests to be suitable for a combination of drugs though because two organisms are cultured it does not follow that both are necessarily responsible for the infection In general it is perhaps better to use the drugs in succession (if the first proves ineffective) than simultaneously

Individual Anti bacterial Drugs

Only those drugs with a wide application will be considered here Quinine and the other anti malarials isonicotinic acid hydrazide para amino salicylic acid emetine antimony the arsenicals the sulphone compounds and other drugs which are only active against one or a few organisms are dealt with under the diseases in the treatment of which they are used

The Sulphonamides

In 1935 Domagh published his discovery that *Prontosil rubrum* a red dye protected mice against streptococcal infection The active part of the drug was shown to be the sulphonamide group and the simple compound sulphanilamide (Prontosil album) $H_2N\langle\rangle SO_2NH_2$ was soon found to be equally effective both in protecting mice and men In addition to streptococci sulphanilamide is active only against *N meningitidis N gonorrhoeae* coliform organisms and *Clostridia* In the following years numerous other sulphonamides were discovered with a wider action and with less toxic effects The antibiotics have now superseded the sulphonamides in the treatment of most infections but the sulphonamides remain valuable in certain circumstances and have the advantages of cheapness rarity of toxic effects and ease of administration

The sulphonamides are bacteriostatic and they are thought to inhibit the multiplication of sensitive organisms by blocking enzyme systems In this way they enable the body s natural defence mechanisms to deal with the infection The individual compounds mainly differ in their rate of absorption and excretion and in their distribution in the tissues

In at least two infections the sulphonamides are still the drugs of choice—namely *E coli* infections of the urinary tract (though a few strains of *E coli* are unresponsive) and meningococcal meningitis or septicaemia Sulphonamides are also thought to be as effective as antibiotics in bacillary dysentery though as this is usually a self limited disease of short duration anti bacterial drugs are of comparatively small importance except as a public health measure to eradicate the sources of infection Pneumonia due to *Strep pneumoniae* usually responds excellently though in view of the frequent uncertainty as to the causative organism of pneumonia and the possibility that *Strep pneumoniae* will be sulphonamide resistant penicillin is in general preferable

There seems to be no advantage in using more than the following three sulphonamides for general use—

Sulphadimidine (Sulphamezathine) This is more rapidly absorbed but more slowly excreted than other sulphonamides and its excreted form is fairly soluble so crystalluria is rare It should be used for *N meningitidis* infections and pneumonia due to *Strep pneumoniae*

For adults an initial loading dose of 3 g should be given followed by 1½–2 g 6 hourly for about 5–7 days Children of up to 1 year should be given a sixth 1–3 years a third and 6–12 years two thirds of the adult dose If the patient is unconscious or vomiting similar quantities of sodium sulphadimidine may be given intravenously or deeply intramuscularly

As a prophylactic to prevent streptococcal infections in those who have had rheumatic fever the dose is 0 5 g 12 hourly indefinitely

Sulphamethizole (Urolucosil) This is highly soluble and toxic effects are very rare It is perhaps the best drug for *E coli* urinary infections and there is no need either to render the urine alkaline or to give a large fluid intake with it The adult dose is about 0 2 g 4 times daily for 5–7 days

Phthalylsulphathiazole This is poorly absorbed from the bowel and is used for bacillary dysentery It is also used for alimentary infections when the causative organism is unknown and for ulcerative colitis in the hope of dealing with secondary infection but is of doubtful efficacy The dose is about 1 g thrice daily for 5–7 days or indefinitely in ulcerative colitis

Toxic Effects. The early sulphonamides frequently

caused nausea headache cyanosis and depression but all these are uncommon with the preparations now used Deposition of crystals in the urinary tract causing haematuria and even anuria occurs occasionally but very rarely with sulphadimidine and probably never with sulphamethizole These renal complications are made even less likely by ensuring a daily fluid intake of at least 1½ litres and maintaining the urine alkaline by sodium citrate 2 g (30 gr) 4 hourly If they nevertheless occur the drug should be stopped and if there is anuria the treatment for this (p 476) should be given

Sensitization to sulphonamides often with a rash and fever is not uncommon It is particularly likely to follow local treatment of skin conditions by ointments containing sulphonamides so such ointments *should not be used The rash is variable but is most* marked on exposed areas of skin If sensitization occurs the drug should be stopped and the patient warned that he should never have sulphonamides again and should inform any future medical adviser of his sensitivity

Very rare but serious toxic effects are those on the bone marrow Agranulocytosis is the least uncommon and others are aplastic anaemia haemolytic anaemia and thrombocytopenia If a patient on sulphonamides develops a sore throat malaise or fever the blood should be examined and if these dyscrasias are found the drug should be stopped and penicillin given until the blood has returned to normal

Acquired Resistance *N meningitidis* infections are rarely if ever resistant to sulphonamides Many strains of most other organisms are now resistant whereas in the early days of sulphonamide therapy resistance by these same organisms was less common They include *N gonorrhoeae Strep pyogenes Strep pneumoniae* staphylococci and *E coli* In particular resistance by *N gonorrhoeae* infections which at first rarely occurred rapidly increased until when penicillin was introduced a high proportion of cases did not respond satisfactorily

Penicillin

Fleming discovered in 1929 that the staphylococci in a culture plate failed to grow around a colony of the mould *Penicillium notatum* with which the plate had been accidentally contaminated He called the substance produced by the mould and responsible for this inhibition penicillin In 1941 Florey Chain and others at Oxford succeeded in isolating it and producing enough for clinical use It is bactericidal in high concentration and bacteriostatic in low concentration

Penicillin consists of a number of complex acids called I II III and K or F G X and K which differ in activity The sodium potassium calcium and procain salts of these acids are used therapeutically The proportion of these penicillins varies and the most active is penicillin II or G One mg of pure crystalline penicillin G contains 1 666 international units Benzyl penicillin BP (soluble or crystalline penicillin or Penicillin G') consists of over 95 per cent of the sodium or potassium salt of penicillin G

A very large number of compounds of penicillin have been made In addition to benzyl penicillin the following are the most useful—

Procaine benzyl penicillin (Procaine penicillin) is the relatively insoluble procaine salt of benzyl penicillin A single daily injection of 600 000 units will give a bacteriostatic blood level for 24 hr

Benzathene penicillin (Penidural) is a long acting compound of benzyl penicillin and NN[1]-dibenzyl ethylene-diamine A single injection of 300 000 units will give a bacteriostatic blood level for 5 days and larger doses will give bacteriostatic levels for 15 days or longer

Phenoxymethyl penicillin (Penicillin V) is given by mouth and produces far higher and more consistent blood levels than other forms of oral penicillin It is prescribed by weight and 125 mg is equivalent to 200 000 units of benzyl penicillin

Absorption Distribution and Excretion Penicillin is quickly absorbed when given intramuscularly When given by mouth a large though greatly varying proportion of all forms of it except phenoxymethyl penicillin is destroyed by the acid in the stomach Phenoxymethyl penicillin is consistently but not wholly absorbed After absorption penicillin diffuses into most places except the serous cavities the cerebro spinal fluid and the anterior chamber of the eye where it appears only in very small amounts There is evidence however that when the barriers to these places are inflamed diffusion of penicillin *occurs more readily so it is effective in such conditions* as meningitis and empyema (though it may also be given directly into the cerebro spinal fluid or the pleural cavity and may be combined with the more diffusible sulphonamides when an appropriate organism is present)

Some 60 per cent of penicillin given by injection appears in the urine Most of this is excreted in the first hour after injection of benzyl penicillin Some 25 per cent of oral phenoxymethyl penicillin appears in the urine

Administration and Dosage It has been widely assumed that a continuous bactericidal level of penicillin is essential or at least is much superior to an intermittent bactericidal level In consequence it was the custom until recently to give penicillin 3 or 4 hourly by intramuscular injection and in the early

situation is provided by infective processes due to a variety of organisms such as peritonitis or lung abscess or other chronic lung infections Although a combination of penicillin and streptomycin has been widely used in both these circumstances with good results it is doubtful whether they are usually superior to a tetracycline alone or in the case of lung abscess to penicillin alone On the other hand the tetracyclines have the objectionable feature of causing alimentary side effects and their widespread use encourages the development of resistant staphylococci They are also very expensive Urinary infections associated with more than one organism may sometimes appear on the basis of *in vitro* sensitivity tests to be suitable for a combination of drugs though because two organisms are cultured it does not follow that both are necessarily responsible for the infection In general it is perhaps better to use the drugs in succession (if the first proves ineffective) than simultaneously

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In 1935 Domagh published his discovery that Prontosil rubrum a red dye protected mice against streptococcal infection The active part of the drug was shown to be the sulphonamide group and the simple compound sulphanilamide (Prontosil album) $H_2N\langle\bigcirc\rangle SO_2NH_2$ was soon found to be equally effective both in protecting mice and men In addition to streptococci sulphanilamide is active only against *N meningitidis N gonorrhoeae* coliform organisms and *Clostridia* In the following years numerous other sulphonamides were discovered with a wider action and with less toxic effects The antibiotics have now superseded the sulphonamides in the treatment of most infections but the sulphonamides remain valuable in certain circumstances and have the advantages of cheapness rarity of toxic effects and ease of administration

The sulphonamides are bacteriostatic and they are thought to inhibit the multiplication of sensitive organisms by blocking enzyme systems In this way they enable the body s natural defence mechanisms to deal with the infection The individual compounds mainly differ in their rate of absorption and excretion and in their distribution in the tissues

In at least two infections the sulphonamides are still the drugs of choice—namely *E coli* infections of the urinary tract (though a few strains of *E coli* are unresponsive) and meningococcal meningitis or septicaemia Sulphonamides are also thought to be as effective as antibiotics in bacillary dysentery though as this is usually a self limited disease of short duration anti bacterial drugs are of comparatively small importance except as a public health measure to eradicate the sources of infection Pneumonia due to *Strep pneumoniae* usually responds excellently though in view of the frequent uncertainty as to the causative organism of pneumonia and the possibility that *Strep pneumoniae* will be sulphonamide resistant penicillin is in general preferable

There seems to be no advantage in using more than the following three sulphonamides for general use—

Sulphadimidine (Sulphamezathine) This is more rapidly absorbed but more slowly excreted than other sulphonamides and its excreted form is fairly soluble so crystalluria is rare It should be used for *N meningitidis* infections and pneumonia due to *Strep pneumoniae*

For adults an initial loading dose of 3 g should be given followed by 1½–2 g 6-hourly for about 5–7 days Children of up to 1 year should be given a sixth 1–3 years a third and 6–12 years two thirds of the adult dose If the patient is unconscious or vomiting similar quantities of sodium sulphadimidine may be given intravenously or deeply intramuscularly

As a prophylactic to prevent streptococcal infections in those who have had rheumatic fever the dose is 0 5 g 12 hourly indefinitely

Sulphamethizole (Urolucosil) This is highly soluble and toxic effects are very rare It is perhaps the best drug for *E coli* urinary infections and there is no need either to render the urine alkaline or to give a large fluid intake with it The adult dose is about 0 2 g 4 times daily for 5–7 days

Phthalylsulphathiazole This is poorly absorbed from the bowel and is used for bacillary dysentery It is also used for alimentary infections when the causative organism is unknown and for ulcerative colitis in the hope of dealing with secondary infection but is of doubtful efficacy The dose is about 1 g thrice daily for 5–7 days or indefinitely in ulcerative colitis

Toxic Effects. *The early sulphonamides frequently*

Desensitization has been successfully achieved by starting a course of injections with some 50 units and then doubling the dose each day until the thera peutic quantity can be tolerated If a reaction occurs the course should be restarted at a level that gives no reaction

Acquired Resistance This chiefly occurs with staphylococci A high proportion of the strains of this organism found in hospitals and a smaller though considerable proportion of the strains found elsewhere are resistant This is one of the strong objections to the widespread use of penicillin as a prophylactic and to its use in minor staphylococcal infections such as boils and styes which clear up quickly without treatment The problem is aggra vated by the fact that an increasing proportion of staphylococcal strains are resistant to most or all other antibacterial drugs

The Tetracyclines

These are tetracycline (Achromycin Tetracyn) chlortetracycline (Aureomycin) and oxytetracy cline (Terramycin) They were all originally derived from various species of *Streptomyces* found in the soil but are now produced synthetically Chlor tetracycline was discovered in 1948 oxytetracycline in 1950 and tetracycline in 1952 They are known as broad or wide spectrum antibacterial drugs because they are active against most pathogenic bacteria and some *Rickettsiae* and viruses They are bacteriostatic not bactericidal

The three tetracyclines have almost the same range of activity and bacteria resistant to one are nearly always resistant to the other two They are well absorbed from the bowel and are always given by mouth except when the patient is vomiting or uncons ious when they may be given intravenously Absorption from the bowel is incomplete and they profoundly change the bacterial flora of the colon They are all far more expensive than penicillin

Because of their toxic effects expense and the tendency of some organisms to become resistant to them the tetracyclines should be used very spar ingly In practice they have been used too freely for the main reason that they can be given by mouth whereas penicillin until recently could be given satis factorily only by injection Now that phenoxymethyl penicillin is available there is no excuse for using the tetracyclines except when there are definite indica tions for doing so Such indications are seen very rarely in Britain

The chief infections which respond particularly to the tetracyclines but not to penicillin or sulphona mides are those due to *Rickettsiae* (in Britain mainly Q fever) *H influenzae* and some *Salmon ellae* brucellosis (though this is also responsive to streptomycin) and lymphogranuloma inguinale and psittacosis both of which are due to large viruses Pertussis also seems responsive if the drugs are given early in the disease but for the ordinary mild case their use is unjustified

Other and less definite indications for the tetracy clines are infections by organisms which are usually responsive to penicillin or sulphonamides but have become resistant to these drugs These include some staphylococcal infections and some infections of the urinary tract The main circumstance in which the use of the tetracyclines is justifiable without know ledge of the organisms concerned is in treating peritonitis since the organisms likely to be present are usually responsive to the drugs It may also be sound practice to give them to pneumonia patients who have failed to respond to penicillin since bacteriological study of the sputum does not neces sarily indicate the organisms responsible Good results have been claimed for them in treating patients with the diagnosis of virus pneumonia but in view of the difficulty of reaching this diag nosis and the good prognosis without treatment these claims are of little value

Chlortetracycline is widely used as an ointment for infective skin conditions So far sensitization re actions have rarely occurred

Administration and Dosage About 16 mg/kg of body weight should be given daily For oral use the drugs are made up in 250 mg capsules and the aver age adult should have a loading dose of 1 g followed by 250 mg 6 hourly or if intravenously 0 5 g twice daily If sodium metaphosphate is mixed with tetra cycline it is more completely absorbed and its blood level increased A smaller dose is therefore needed and the alimentary toxic effects are lessened

Toxic Effects. Nausea and vomiting are common and probably due to the direct action of the drugs on the stomach they can be lessened by giving the drugs with food or milk The other alimentary toxic effects seem to be due to a change in the bowel flora The mouth and anus may be infected by *Can dida albicans* or other fungi causing a sore mouth or pruritis ani 1 per cent gentian violet applications may lessen these symptoms Some increase in the bulk of the faeces is universal and diarrhoea is common Occasionally superinfection of the bowel with resistant staphylococci occurs with consequent severe and sometimes fatal entero-colitis In the worst cases there are cholera like symptoms col lapse and electrolyte disturbances The drug should be stopped and the stool organisms studied as soon as possible to indicate which antibacterial drug will best control the infection This is often erythro mycin which should be given immediately if the patient s condition is very bad Parenteral fluid and

days it was given by continuous intramuscular or intravenous drip This assumption encouraged the search for long acting injectable penicillins But there seems to be no convincing evidence that continuous bactericidal levels are always important On the other hand when organisms are comparatively insensitive or inaccessible (as in bacterial endocarditis infections of serous cavities boils or walled off collections of pus) there is evidence that intermittent very high blood levels as are obtained by giving 1 million units of benzyl penicillin twice daily are more effective than the continuous moderate level obtained by giving the same total quantity in 6 or 8 doses

The dosage of penicillin may be influenced by the following factors (1) the nature of the infective process (2) the species of organism isolated (3) the *in vitro* sensitivity of the organism (4) the response to initial treatment In addition there is the important practical consideration that ill effects from a high dosage of penicillin are unknown sensitization reactions occurring irrespective of the dose When the patient has a grave infection therefore it is justifiable to give a dose which is probably far larger than is needed

As already suggested a high dosage of penicillin is indicated when the infective process is thought to be inaccessible to the drug as in empyema boils and carbuncles meningitis and infective endocarditis

Some species of bacteria are always highly sensitive to penicillin These include *Strep pyogenes Strep pneumoniae N gonorrhoeae N meningitidis* and *Treponema pallidum* Others such as the coli typhoid group are always insensitive The important species whose sensitivity varies are the staphylococci and *Strep viridans* though infections due to staphylococci which are resident *in vitro* sometimes seem to respond satisfactorily

When the infection fails to respond to penicillin the patient may then be given (1) no anti bacterial drugs (2) an increased dose of penicillin or (3) another anti bacterial drug If the infection is grave the first course cannot be taken The decision between the other two courses depends on the circumstances If the organism which is certainly responsible for the infection has been isolated and found insensitive to penicillin but sensitive to another drug a change to this other drug is obviously indicated When there is uncertainty about the responsible organism (as in pneumonia) a change to another drug probably one of the tetracyclines is also indicated When the *in vitro* tests suggest that the organism is comparatively insensitive to penicillin but is no more sensitive to the other drugs or when there are reasons for preferring a bactericidal to a bacteriostatic drug an increase in dose should be given

The maximum dose of parenteral penicillin is about 2 million units daily usually given in 2 or 3 doses *It is probably unwise to give less than about* 500 000 units daily though in practice many infections respond to far less The dose of phenoxymethyl penicillin for oral use is about 125 mg (equivalent to 200 000 units) to 250 mg 4 hourly This is probably the preparation of choice in most circumstances

The duration of the course of penicillin depends on the situation As a rule it should be stopped a few days after the infection has subsided but sometimes the course should be for far longer and sometimes for less Infective endocarditis demands a course of a month or more gonorrhoea may be cured by a single injection of 500 000 units

Penicillin has been widely used locally As a solution in water it may be injected in serous cavities or intrathecally instilled into the nose ears or eyes and applied to open wounds or to infected skin conditions It may also be applied to the skin in creams or ointments or to the mouth and throat in lozenges The local use of penicillin may bear some responsibility for the increase in resistant organisms in recent years and there is no doubt that sensitization reactions are likely to follow prolonged local use The value of much of this local treatment is moreover uncertain and lozenges in particular are probably useless as a rule Intrathecally penicillin is irritating to the meninges In general parenteral or oral therapy should be preferred to local and if local applications are given the duration of treatment should not exceed some 5 days in order to lessen the likelihood of sensitization

Toxic Effects Penicillin never causes toxic effects except by direct irritation of the meninges or a few other structures or by rendering patients sensitive to it Sensitization may result in various allergic *manifestations The commonest is urticaria which* is usually mild but is occasionally very severe and persistent and may even lead to exfoliative dermatitis If it develops the penicillin should if possible be stopped The urticaria should be treated by anti histamine drugs or if severe by cortisone up to 300 mg daily and under cover of these drugs penicillin administration can sometimes be continued Severe anaphylactic shock with asthma has been described occasionally and some cases have been fatal It should be treated by adrenaline in the same way as other varieties of asthma Sensitization seems to be far less common after oral than after parenteral penicillin

The patient who is found to be sensitive to penicillin should always be warned of this state so that he can in turn warn any doctor he sees in future

about 3 to 4 weeks but with 1 g daily the incidence is less than 20 per cent and the symptoms rarely begin until after 6 weeks and are usually mild Renal insufficiency greatly increases the liability to vestibular damage as streptomycin is excreted by the kidneys so the blood level is higher Smaller doses should be given to those so affected and assessed by estimating the blood concentration which should not exceed 25 μg/ml

The only other important toxic effects of streptomycin are the sensitivity reactions which are common after prolonged contact with the drug Those who constantly handle it are very liable to skin eruptions and should therefore take great care to avoid getting it on their skin by using rubber gloves Patients are less likely than handlers to become sensitized but they occasionally develop severe anaphylactoid reactions or fever as well as skin eruptions These reactions can be suppressed partially or completely by the simultaneous administration of anti histamine drugs or cortisone Desensitization can sometimes be effected by starting a course of twice daily injections with a minute dose (as little as 10 μg) insufficient to cause a reaction and steadily increasing the dose with temporary decrease if there is a reaction until the therapeutic quantity can be given without ill effect Anti histamine drugs should be given during this course

Acquired Resistance All sensitive bacteria can easily become resistant to streptomycin This is thought to be due both to the multiplication of strains which are already resistant and to genetic mutations which in a single step may produce bacteria immune to concentrations of streptomycin vastly greater than those lethal to the original organism Acquired resistance is a potential problem when the drug is given for long periods In practice this should apply only to bacterial endocarditis and tuberculosis and in the latter case the problem can be solved by always combining the streptomycin with para aminosalicylic acid or isonicotinic acid hydrazide

Erythromycin

The anti bacterial spectrum of erythromycin is similar to that of penicillin though it is predominantly bacteriostatic in action It was isolated in 1952 from *Streptomyces erythreus* It diffuses freely into all body fluids except the cerebro spinal fluid is well absorbed when given by mouth and has few toxic effects Most bacteria especially the *Staph aureus* readily develop resistance to it but cross resistance to other anti bacterial drugs does not occur *In vitro* experiments suggest that the action of erythromycin is synergistic with that of streptomycin antagonistic to that of penicillin and does not influence that of the tetracyclines

In practice the main use of erythromycin is in treating penicillin resistant *Staph aureus* infections Because of the increasing problem of resistant organisms in hospitals the suggestion has been made which has much to recommend it that the drug should be used for no other purpose Another possible use is in treating penicillin sensitive infections in patients who have become sensitized to penicillin

Administration and Dosage For adults the oral dose is 0 3 to 0 5 g 6 hourly and for children 30 mg/kg of body weight daily divided into 4 equal doses As an alternative to tablets there is a suspension for children Severely ill patients who cannot swallow may be given the drug parenterally An ointment is available for superficial skin infections

Toxic Effects These are uncommon and usually mild Diarrhoea occasionally occurs though much less often than with the tetracyclines Vomiting and pruritis ani are also described

Neomycin

The anti bacterial spectrum of neomycin is the widest known It is the only broad spectrum anti bacterial drug which is bactericidal rather than bacteriostatic It was discovered in 1947 *In vitro* it is particularly effective against *Staph aureus* and *Salmonella* and is the best drug available for most species of *Pseudomonas* though some are resistant to it It is relatively ineffective against streptococci especially *Strep viridans* Acquired resistance to neomycin rarely if ever occurs It is hardly absorbed from the bowel

Because parenteral neomycin may cause deafness and renal damage it should be used only for potentially lethal infections by organisms which are sensitive to no other drug In practice such infections are extremely rare Neomycin may however be used with little or no risk by aerosol orally and topically By aerosol it may be useful for chronic lung infections not responding satisfactorily to other drugs Orally it may be used preoperatively to diminish the bacterial flora and for alimentary infections due to organisms resistant to other drugs Perhaps its greatest value is in topical applications for various skin infections

Administration and Dosage The adult intramuscular or oral dose is 0 5 g 6 hourly As an aerosol the dose is about 250 mg 12 hourly For topical use neomycin should be dissolved in water or saline in a concentration of 1 mg/ml and a thin dressing over the affected areas kept moist with this solution

electrolytes may be needed It has been hypothesized that some of the ill effects of the tetracyclines are immediately due to vitamin B deficiency consequent upon destruction of vitamin synthesizing bacteria in the bowel Although such bacterial destruction may well occur it is hardly credible that this should cause a sore mouth due to vitamin deficiency within a few days

Toxic effects other than alimentary are uncommon Jaundice has occurred but only after intravenous therapy Sensitization reactions are very rare

Acquired Resistance The main organism which has developed resistance is the staphylococcus More than 50 per cent of hospital strains may be resistant Occasionally there is also cross resistance to chloramphenicol

Chloramphenicol (Chloromycetin)

The range of activity of chloramphenicol is similar to that of the tetracyclines and it is also given by mouth It is bacteriostatic not bactericidal Resistance to it can be acquired by many organisms and cross resistance with the tetracyclines occurs occasionally It was discovered in 1947 and at first was prepared from *Streptomyces venezuelae* but soon afterwards was synthesized

Because it has caused fatal aplastic anaemia it should not be used except when clearly superior to other anti bacterial drugs The only infections of which this is generally true are typhoid and para typhoid fevers Otherwise its prescription should wait upon laboratory tests which have indicated that the causative organism is more sensitive to it than to anything else

Administration and Dosage An initial dose of 1 g followed by 250 mg 6 hourly should be given for not longer than 10 days For severe infections it is justifiable to give about double this amount

Toxic Effects Chloramphenicol is more completely absorbed from the bowel than are the tetracyclines and gastro intestinal side effects are less common Its one serious side effect is aplastic anaemia of which many cases have been described several fatal In most cases this has followed prolonged heavy dosages or repeated short courses for such relapsing conditions as bronchiectasis or urinary infection However some cases have followed ordinary dosage sometimes after a long interval though these seem to be very rare and their likelihood has perhaps been exaggerated

Streptomycin

The second important antibiotic to be discovered was streptomycin, which was isolated in 1944 by Waksman from *Streptomyces griseus* It is bactericidal in high concentration and bacteriostatic in low concentration It is a water soluble base and its sulphate salt is the one commonly used It is not absorbed from the bowel and is given by intra muscular injection except when intended to destroy organisms in the bowel Therapeutic levels in the blood persist for 6–12 hr after a single injection of 1 g It passes freely into the ascitic or pleural fluids but not into the cerebro spinal fluid in effective amount It is excreted in the urine where it is greatly concentrated

Streptomycin is active against many organisms but because of its toxic effects and the rapidity with which most organisms become resistant to it its practical use is severely limited Its supreme value is in treating all forms of tuberculosis in combination with para amino salicyclic acid (P A S) or isonicotinic acid hydrazide (isoniazid) These three drugs have completely changed the outlook in tuberculosis especially its severe and acute forms Most patients with miliary tuberculosis now make a complete recovery in the past nearly all died quickly Streptomycin is also valuable for some Gram negative urinary tract infections resistant to sulphonamides (especially those due to certain strains of *E coli* and *Proteus*) some *H influenzae* infections and Friedlander pneumonia It should rarely be given alone for non tuberculous infections except after *in vitro* tests have indicated that an organism is sensitive to it It may be combined with penicillin in treating lung infections or peritonitis in which several organisms seem to be playing a part and in treating bacterial endocarditis Moreover penicillin and streptomycin may sometimes be synergistic

Administration and Dosage For tuberculosis the dose is 1 g (children 40 mg/kg of body weight) daily for up to many months along with P A S or isoniazid For infective endocarditis 1 g daily should be given for a month with penicillin and for acute urinary and other infections 1 g 12 hourly for about 5 days

Toxic Effects The chief toxic effect of streptomycin is to the vestibular nerve The main symptoms of this are ataxia and giddiness and there may also be tinnitus and some deafness If the drug is stopped when the symptoms begin there may be complete recovery but in severe cases there is permanent damage though the disability may be overcome in time Dihydrostreptomycin is much more liable to cause permanent loss of hearing than streptomycin and as it has no advantages should never be used The damage is more frequent and severe in the elderly and its incidence is directly proportionate to the dose and duration of treatment When 2 g daily are given most subjects develop the symptoms in

THE RELIEF OF PAIN

The symptom most often requiring relief is pain The best treatment for pain is the radical removal of its cause but in practice this is rarely possible Even when radical treatment is available there is usually a need for pain relieving measures as well The patient with pneumonia and painful pleurisy should be given penicillin but he should also be given an analgesic drug

Severe pain is in general a sufficient ground for the immediate administration of an analgesic drug But an effect of the drug may be to obscure the diag nosis Frequently this does not matter but when the patient has an acute abdominal disaster if the diag nosis is obscured the surgeon may fail to do a neces sary op ration But provided he knows the drug has been given he is unlikely to be misled and if the pain is severe enough the risk of misleading him must be taken

The severity of pain is governed not merely by the local lesion from which it arises but also by the mind of the victim The phlegmatic subject is less pain-conscious than is the sensitive and we are all more aware of pain when anxious and depressed than when care free and elated In so far as pain is mental it is little if at all relieved by analgesic drugs Indeed the failure of these drugs is a useful diag nostic pointer by suggesting that pain is more mental than physical

Pain has other important emotional aspects The problem of pain has been written and talked about throughout the ages often in relation to religious beliefs Men have always been proud of suffering pain with fortitude In primitive societies youths are often initiated into manhood by being branded or tortured in other ways without flinching or murmur ing The suffering of the sick causes great emotional repercussions on other people Pain is often alleged to have a purifying effect upon the spirit The idea was once common and perhaps now is not dead that pain especially in childbirth was given by the Almighty and to relieve it is contrary to His wishes There was strong opposition to giving anaesthetics in labour when this was first advocated Although the public is wedded to the bottle of medi cine there is no universal approval of measures to relieve pain The medicines which do this are thought to be drugs and a drug is believed to be an inherently vicious substance Some people habitually reach the conclusion that others make an unnecessary fuss about their pain and that to give them repeated doses of drugs is to pander to them Medical men and nurses sometimes take this atti tude for those who are constantly in contact with people in pain are apt to become increasingly in different to their distress

Because of these emotional aspects of pain many people who could be given relief fail to have it Those with rheumatoid arthritis or recurrent head aches who are greatly helped by aspirin may say that they do their best to avoid taking it Patients in hospital often say nothing about their pain and perhaps in consequence have sleepless nights When asked leading questions they may admit to having pain but say that they did not complain because they hated to make a fuss

Long standing and persistent pain usually cannot be relieved by analgesic drugs and frequently it is more mental than physical But efforts should be made to overcome the emotional hindrances to analgesia when pain is due to acute illnesses in juries and recurrent disorders A matter of fact and unemotional attitude is best The patient s winsome remark Don t bother about me doctor it doesn t hurt much and it will soon be over should be re ceived not with admiration for his fortitude but with the rejoinder that it is foolish to suffer unneces sary pain When pain seems severe it is probably best to order an analgesic regularly such as aspirin 1 g 4 hourly not merely when the patient asks for it

Analgesic Drugs

The simplest method of relieving pain is nearly always by the non specific analgesic drugs and as a rule this is the method of choice The number of these drugs is very great and new drugs are being constantly introduced

The aromatic group of analgesics include aspirin (acetylsalicylic acid) and other salicylates phena cetin and amidopyrine Aspirin is usually very effec tive in relieving headache and rheumatic pains As a rule it is dangerous only if taken in very large doses when it is apt to cause tinnitus deafness and vomiting In ordinary dosage it occasionally causes nausea and other dyspeptic symptoms though if a patient complains that aspirin upsets him this is not necessarily true if given an aspirin mixture of whose composition he is ignorant he may not be upset A few people are sensitive to aspirin and develop asthma urticaria and other allergic re actions Rarely it causes haematemesis especially when taken on an empty stomach Calcium aspirin is less likely to cause trouble than ordinary aspirin The dose i in the order of ½ to 1 g (10 to 15 gr)

Toxic Effects Some 10 per cent of patients who are given neomycin parenterally develop progressive deafness though total loss of hearing is not invariable Although the drug is stopped as soon as the deafness begins later improvement in hearing does not occur The first signs of renal damage are albuminuria and urinary casts and nitrogen retention and oliguria may follow The renal damage is reversible after the drug is stopped These effects do not seem to follow aerosol oral or topical treatment

Polymyxins

Five polymyxins known as A B C D and E are known all derived from species of the *Bacillus polymyxa* and first discovered in 1950 Their anti bacterial spectrum is narrow as they are active only against Gram negative rods except *Proteus* They are the most effective drug for *Ps pyocyanea* infections and they are also effective against *E coli A aerogenes H influenzae* and *Shigella* infections They have a rapid bactericidal action and organisms do not develop resistance to them They are not absorbed from the bowel They do not seem to be antagonistic to other anti bacterial drugs and may therefore be used satisfactorily in combination when there are mixed infections They are very expensive

Polymyxins A C and D are liable to cause renal damage so polymyxins B and E are always used in practice as they do not have this effect For systemic use they are best given intravenously as intramuscular injections are apt to be painful They may be used by mouth in high dosage for alimentary infections and they may also be given intrathecally or applied locally to the skin nose ears or conjunctivae

Administration and Dosage The adult intravenous or intramuscular dose is about 250 000 units 4 hourly and for children 10 000 units/kg of body weight 4 hourly The oral dose is 1 million units 4 hourly For local application a 0 1 to 1 per cent solution or cream may be used

Toxic Effects Polymyxins B and E do not cause serious toxic effects Pain and inflammation at the site of injection accompanied by malaise and fever may follow intramuscular administration There seem to be few ill effects from intravenous or local administration

Bacitracin

The anti bacterial spectrum of bacitracin is fairly wide and includes all streptococci all staphylococci and the *Clostridia* It is bactericidal It was first discovered in 1947 Commercial preparations are not pure so its dose is measured in units Pure bacitracin is thought to contain 66 units/mg It is not absorbed from the bowel and for systemic use must be given parenterally It may also be given locally and is well tolerated in all body cavities It seems to have a synergistic action with neomycin The earlier preparations were liable to have toxic effects on the kidney but this is uncommon with modern preparations

The chief indications for bacitracin systemically are severe infections by staphylococci and other organisms which have become resistant to penicillin and the tetracyclines In practice it is mainly used locally as in the treatment of ulcers and burns particularly when mixed infections are present

Administration and Dosage The intramuscular dose is 10 000 to 20 000 units for adults (200 units/kg of body weight for children) 6 or 8 hourly Locally it is used in solution containing 500 units/ml or ointment containing 500 units/g

Toxic Effects Sensitization rarely if ever occurs The only serious toxic effect is renal damage but this is now uncommon and is thought to be made less likely by keeping the urinary output above 1 litre daily Pain after the injections is common but can be lessened by giving them with procaine There may be anorexia nausea and vomiting

Novobiocin (Albamycin)

The anti bacterial spectrum of novobiocin is similar to that of penicillin and it is bactericidal It was isolated in 1956 from *Streptomyces niveus* It diffuses freely into all body fluids except the cerebro spinal fluid and is well absorbed by mouth Resistance to it can develop especially by *Staph aureus* but there is no cross resistance with penicillin the tetracyclines or erythromycin

The main practical use of novobiocin seems to be in treating resistant staphylococcal infections It may also be used for penicillin sensitive infections in patients who have become sensitized to penicillin *Proteus* infections are sometimes more susceptible to novobiocin than to anything else

Administration and Dosage For adults a loading dose of 1 g followed by 0 5 g twice daily may be given and for children 5 mg/kg weight 8 hourly

Toxic Effects So far very few toxic effects have been reported A yellow pigmentation occurs sometimes but this is due to a breakdown product of the drug and seems to be harmless Mild nausea and diarrhoea may occur Sensitization with skin rashes is seen occasionally

wholly condemn a remdey (*see* p 31) but it calls for great restraint in using complicated procedures which involve repeated visits to hospital and which encourage the conviction of invalidism In general there is little objection to these methods if they are simple and inexpensive But for severe pain they are of doubtful utility and analgesic drugs will be needed

Intractable Pain

When pain is very severe and persistent yet pre dominantly determined by an organic process the methods of relief so far considered may be insuffi cient If they are sufficient this may be at the ex pense of causing mental dullness depression and addiction as the consequence of large doses of an opium derivative or a powerful synthetic analgesic An important cause of pain of this kind is wide spread and especially osseous malignant deposits Here as the patient is dying addiction matters little and to dull his mind may be to do him a kind ness But when the lesion is benign these secondary effects are a grave disadvantage Examples of benign lesions causing intractable pain are those responsible for trigeminal neuralgia post herpetic neuralgia and causalgia following amputation of a limb

In these circumstances surgical measures to relieve pain may be considered and these are equally applicable to pain due to malignant disease when the patient seems likely to have a reasonable span of life The simplest of these measures is alcohol injection of the appropriate nerve trunks or ganglia The nerve trunks may also be divided as in treating trigeminal neuralgia These measures do not give unqualified success and they may have unpleasant ill effects The subject who has had his 5th nerve root divided for trigeminal neuralgia is always left with a numb face on the affected side which is un comfortable and he may develop corneal ulceration or progressive ulceration of the nose A more serious surgical procedure is the division of the spino thalamic tract in the spinal cord Even if damage to the other pathways is avoided which is not easy the operation is not invariably successful and is always followed by the loss of pain sense over half the body below the level of the section Finally pre frontal leucotomy may be employed This may so alter the patient s attitude to pain that although he is still aware of it he is largely relieved of the suffering which is its emotional component This relief tends to pass off after some months so the operation is more suitable for those with malignant disease than for those with non malignant states To be effective for long periods the leucotomy has to be so extensive that the subject s personality is adversely affected The drug chlorpromazine (Lar gactil) apparently has an effect similar to that of leucotomy in making patients less aware of pain Although its success is limited it has obvious advan tages over leucotomy and may be well worth a trial The initial dose is about 25 mg thrice daily which should be gradually increased until the most satis factory result is achieved The maintenance dose is usually between 50 and 100 mg thrice daily

The I sychological Approach to Pain

The highest level at which pain may be relieved is the psychological Some people especially mem bers of certain races seem to have the power of so changing their reactions that they suffer little pain from most unpleasant stimuli The Indian fakir who lies on his bed of nails is a familiar example The subject of an hysterical trance may have his eyeballs pressed upon or his Achilles tendon squeezed with out showing any visible sign that he is being hurt For many years hypnosis has been employed occasionally to relieve pain Teeth have been drawn babies have been born painful dressings have been made painless and even major abdominal opera tions have been done under its influence

Not enough attention has been paid to this psychological approach In particular hypnotic methods have been considered as improper and un professional and they have tended to be the pro vince of the charlatan There is now much less objection to hypnosis on grounds of principle than in the past It is time-consuming and expensive and therefore hardly applicable to pains of short dura tion But it could perhaps be of great practical help in treating the recurrent and persistent pains of a considerable proportion of people

Psychogenic Pain

Perhaps the most intractable of all pain is that which is predominantly determined by psychological fac tors Such pain is common Its chief characteristics probably are (1) It is often very persistent or con tinuous even for months or years at a stretch (2) It is unrelieved or little relieved by analgesic drugs (3) It tends to be widespread and symmetrical (4) It is often described in bizarre terms such as

taken up to 3 or 4 hourly though much larger doses can be given Phenacetin has an analgesic effect similar to aspirin and with the addition of caffeine is widely used in combination with it as the tab or mist A P C (aspirin phenacetin and caffeine) It is much less likely to cause gastric up sets than aspirin but sometimes gives rise to methaemoglobinaemia with consequent cyanosis Amidopyrine although very effective occasionally causes agranulocytosis which may be fatal so should not be used

The opium group of alkaloids are most powerful analgesics and opium has been used to relieve pain for many centuries All are liable to cause addiction and their use is restricted by the Dangerous Drugs Acts Morphine is the most popular in doses of about 10 to 30 mg (¼ to ½ gr) It is a powerful respiratory depressant and may be fatal to very ill subjects whose bronchial tubes contain much sputum It frequently causes nausea and vomiting Diamorphine (heroin) is often claimed to be the most effective of all analgesics for intense pain though the value of such claims if depending on nothing more than clinical impressions is small It is less liable to cause vomiting than morphine but is said to lead to addiction more readily The maxi mum pharmacopoeial dose is 8 mg (⅛ gr) Dihydro morphinone (Dilaudid) has a shorter action than morphine and is less likely to cause vomiting The average adult dose is 2–4 mg (1/32–1/16 gr)

Many synthetic analgesics have been introduced in recent years and have to some extent replaced the opium derivatives Widely used examples are pethi dine methadone and phenadoxone They may all cause addiction occasionally though probably much less often than the opium derivatives and all are scheduled under the Dangerous Drugs Acts Pethi dine is probably less powerful than morphine but more powerful than the aromatic group As well as having a general action it also has an anti spasmodic effect on smooth muscle making it a valuable remedy for colic It sometimes causes nausea vomit ing and dizziness The effective adult dose is about 100 mg Methadone (Physeptone) seems to be nearly as effective as morphine as a rule and is less likely to cause narcosis and vomiting Its side effects in clude dizziness nausea and sweating It is effective in alleviating cough by its depressing effect on the cough centre The adult dose is about 10 mg Phena doxone (Heptalgin) is chemically similar to amidone and has a similar analgesic effect and possibly fewer side effects The oral dose is about 5–30 mg and when given by injection 10 mg

Occasionally pain can be relieved by a drug having a specific effect on its cause The alkalies are more effective in relieving the pain of peptic ulcer than the non specific drugs and they rarely have un pleasant side effects (To some extent alkalies may be specific in that they actually encourage ulcers to heal) Atropine and similar compounds relieve the pain of colic through their effect of diminishing smooth muscle tone though they are probably not so useful in this way as pethidine or other non specific analgesics

Local Methods of Relieving Pain

Pain thought to arise from soft tissues (such as the so called fibrositis) tendons and joints is often treated by local measures applied at its site Procaine may be injected into tender areas or painful arthritic joints sometimes with striking immediate relief which may be prolonged far beyond the duration of the effect of the procaine The explanation of this prolonged effect is by no means obvious Perhaps in some cases it lies in the breaking down of adhesions through the increased movement allowed by the temporary alleviation of pain If procaine seems to cause prolonged relief of pain which later returns further injections at suitable intervals may be continued indefinitely

A time honoured method of relieving pain by local procedures is through the mechanism of counter irritation Heat in the form of hot fomentations and poultices hot water bottles or a hot fire is used on a great scale in the home and infra red lamps and short wave diathermy are used in physiotherapy departments Cold is also used widely especially in the treatment of sprains and bruises Numerous chemical substances are applied or rubbed into the skin chiefly in the form of lini ments Linimentum methyl salicylatis B P C in particular is used by athletes for rubbing on their bruises and by old people for rubbing on their osteo arthritic joints In so far as these methods are effec tive they probably work through the same mechanism—namely by causing the release of a histamine like substance which is responsible for reddening and whealing

Procedures of this kind have a great appeal to the public especially to those who dislike the idea of relieving pain merely by drugging To the average man it seems obvious that if some part of him is painful treatment should be applied directly to this part But it is extremely difficult to assess the amount of relief so given and to differentiate between the relief due to a local effect and that due to the effect of suggestion Often the suggestive effect is without doubt important This does not

action and the less stable a short action so an appropriate one can be picked When the main trouble is difficulty in getting off to sleep a short acting compound should be given when the problem is too early awakening a long acting compound is indicated Phenobarbitone (Luminal) is usually unsatisfactory as a hypnotic its chief value being as a regular drug taken throughout the day in small dosage in the treatment of epilepsy and possibly of emotional disorders If given in sufficient amount to cause sleep it is liable to leave the patient drowsy next morning Barbitone (Veronal) is slowly eliminated cumulative and should not be used

Very few people are upset by barbiturates in correct dosage Allergic reactions usually rashes occur occasionally The chief trouble associated with them is overdosage at present they provide one of the most popular means of suicide The fatal dose is usually at least 10 times the average hypnotic dose Barbiturates are ineffective as analgesics except in quantities sufficient to cause deep drowsiness

The most generally valuable long acting barbiturates for use as hypnotics are barbitone sodium BP (Medinal) dose about ½ g (5–10 gr) methyl phenobarbitone BP (Phemitone Prominal) dose 60 to 180 mg (1–3 gr) and allobarbitone BPC (Dial) dose 60–180 mg (1–3 gr) Satisfactory compounds with an intermediate action are amylobarbitone BPC (Amytal) dose 100–300 mg (1½–4½ gr) butobarbitone (Soneryl) dose 100–200 mg (1½–3 gr) and cyclobarbitone (Phanodorm) dose 200–400 mg (3–6 gr) Useful short acting compounds are pentobarbitone (Nembutal) dose 100–200 mg (1½–3 gr) and quinalbarbitone sodium (Seconal) dose 100–200 mg (1½–3 gr)

Among the other hypnotics which may suit some individuals or some special circumstances better than the barbiturates are the following—

Chloral Hydrate This drug is safe and has few after effects in a dose of 1–2 g (15–30 gr) It seems particularly useful for children and infants in a dose of about 200 mg (3 gr) at 1 year It is often given along with bromide in the familiar two fifteens mixture (1 g or 15 gr of each) but the bromide is best omitted since it has little effect until after several days when it is apt to cause drowsiness during the day time The chief disadvantages of chloral hydrate are its unpleasant taste (and this cannot easily be disguised because it has to be given in solution) and sometimes its irritant effect on the stomach

Paraldehyde This is a traditional remedy for confused patients and used to be employed widely in mental hospitals It is safe and effective in doses of 2–10 ml (30–150 minims) by mouth or intramuscularly Its chief disadvantage is its unpleasant taste and smell

Alcohol This is the traditional domestic hypnotic Although usually given without medical advice it can usefully be prescribed for people who have no prejudices against it but are prejudiced against drugs It has the theoretical advantage of providing calories as well as sedation but this is rarely of practical significance

Carbromal This is a bromine derivative of urea In doses of 0 6–1 3 g (10–20 gr) it is a satisfactory hypnotic

PLACEBOS

A placebo may be defined as a remedy which is prescribed not on account of its constituents but on account of its suggestive effect on the patient s mind Discussion about this matter is made difficult by the lack of agreement as to which remedies are placebos One doctor may believe that tonics vitamin mixtures galvanism and faradism have a real effect on the course of illnesses another will believe that they are mere placebos (except as regards vitamins in the very rare circumstances when there is vitamin deficiency) It will be assumed here that the intention behind the remedy is to do no more than act as a placebo The main reason why such remedies are given is usually to do no more than satisfy the patient s desire for a bottle of medicine But the suggestion is sometimes made that placebos play a useful part in treatment

Some strongly condemn placebos as mere quackery others are convinced by their long experience that they may play a valuable part Perhaps the latter believe themselves to be the practical men and they attack the scoffers as being mere theorists—often professors who work among the clinical material of hospital medical schools not among ordinary people in the harsh circumstances of general practice But no convincing evidence of the long term value of placebos derived from large scale controlled series over the course of years has been produced Indeed it is not easy to see how satisfactory control could be achieved The matter must therefore largely be considered from a theoretical angle

The essential defence of placebos is that if a man is convinced some remedy is doing him good it does him good If the criteria by which the good is assessed are the symptoms this may sometimes be

like nails being driven in (5) It is usually accompanied by numerous other bodily symptoms (6) It may be accompanied by overt evidence of psychological disorder (7) There is often no sign of a local organic cause for the pain (but even when there is some local lesion the pain may still be predominantly psychological in origin)

In practice the most important therapeutic aspect of psychogenic pain is to recognize it This at least will prevent unwise surgical procedures No doubt the reason for the intractability of much psychogenic pain is that it has a purpose Occasionally this purpose is the obvious one of increasing the payment given as compensation for an injury but usually it has a more subtle basis The subject may crave for sympathy and develop pain to get it or his pain may enable him to forget his mental anguish

Psychogenic pain may be thought peculiarly suitable for treatment by the psychological approach but this is not so Ordinary methods of reassurance explanation and encouragement usually have little effect and hypnosis is less likely to be successful than in treating pain whose cause is predominantly organic Moreover if psychogenic pain is removed the patient s mental state may be made worse The man who is 'cured of his pain but then commits suicide provides a poor therapeutic result The most favourable subject with predominantly psychiatric pain is the man made anxious by it He may fear that an innocent rheumatic pain is due to cancer and the more he worries about the pain the worse does it become If his fear can be removed as it often can there is every hope that he will stop being aware of pain (*see* p 50)

TREATMENT OF INSOMNIA

Insomnia is often a feature of acute illnesses and may be immediately due to pain or other symptoms of an illness Frequently the insomnia can be relieved by relieving the other symptoms If it nevertheless persists a hypnotic drug should be given and since it will be needed only temporarily there is little objection to its use The man who has suffered some acute psychological disaster should also be given a hypnotic drug Insomnia in these circumstances presents a simple problem

Persistent insomnia tends to be of two kinds first inability to get to sleep and second habitually waking up very early and being unable to sleep again Both kinds of insomnia are often accompanied by the complaint that the sleep which does occur is of poor quality and is associated with restlessness and nightmares Insomnia victims are frequently but not always nervous and worrying individuals

Most of those who seek medical advice on account of habitual insomnia have already tried out such well known remedies as reading a soporific book in bed taking a warm drink before retiring counting sheep and making a conscious effort to relax all the muscles of the body It is nevertheless wise to discuss these measures and occasionally a patient may thereby be helped The next step is to discuss with the patient his views as to the significance of insomnia There is a common belief that all people need a standard minimum of sleep for their health s sake the often stated figures being 7 hr for a man and 8 hr for a woman It is also widely thought that shortage of sleep may cause various disasters such as mental breakdowns insanity and even tuberculosis and other bodily diseases (The victims of pulmonary tuberculosis are habitually told they should have plenty of sleep for the rest of their lives which implies that if they do not they will suffer a relapse) There is no evidence for all this and patients can be reassured The act of reassurance may sometimes improve the insomnia because worrying about it may make it worse Indeed some people easily fall off to sleep in a chair when they have no intention of doing so but when they go to bed sleep eludes them because they fear that it will

Hypnotic Drugs

The decision as to whether the subject of habitual insomnia should be given hypnotic drugs is difficult Many people dislike the idea of taking these drugs even more than they dislike taking analgesics They fear that they will become used to a small dose and will have to take increasing quantities until they end as addicts unable to sleep without their drug Among stable individuals such fears are usually groundless This should be pointed out and it should be emphasized that because drugs are taken for a time it does not necessarily follow that they will always be needed It should also be said that hypnotics do not make people sleepy or stupid during the day or have other deleterious effects In general if someone regularly misses much sleep and spends long hours tossing about in bed there are good grounds for trying a hypnotic drug

The number of hypnotic drugs is very large The most widely used are the barbiturates of which a vast number are known and 12 or more are in common use in Britain They are of varying degrees of stability the more stable have a prolonged

disease but has obvious psychological disorder the *possibility of psychotherapy is more easily remembered*

A good deal of the simple psychotherapy recommended here is no more than common sense and common courtesy To explain to a patient why he needs investigating what his examinations and investigations have revealed and why he has symptoms seems obvious quite apart from any consideration of the body-mind relationship But even these obvious steps may be overlooked with the result that the patient s uncertainty and anxiety are increased Moreover in spite of all the literature of recent years devoted to psychiatric aspects of medicine the view is still widespread among consultants and specialists (though perhaps not among general practitioners) that psychological matters though no doubt important, are not their concern They tend to study humanity in blinkers If they are ophthalmologists they may look at what is visible through an ophthalmoscope if ear nose and throat surgeons at what can be seen through an auriscope or laryngoscope and if gynaecologists at what is revealed by the vaginal speculum Their patients are denied that explanation reassurance and encouragement which can make such a difference to their welfare

Assessing the Value of Psychotherapy

In studying patients with organic disease precise and objective yardsticks such as life and death the duration of fever or the disappearance of X ray shadows can often be used to assess the value of treatment (Even here these objective yardsticks do not provide the whole answer for the patient is not immediately concerned with them but with his symptoms The subject of hallux valgus who has had an operation may be left with a most shapely foot which objectively contrasts most favourably with the deformity and the bunion he had before but this gives him little satisfaction if his foot is so painful that he can hardly walk on it) When assessing the value of psychotherapy the symptoms are often the only yardsticks available and they necessarily lack the precision of objective manifestations Sometimes it is true objective effects more or less reflect the state of mind Gross hysterical states may produce a paralysed limb or the skin lesions of dermatitis artefacta Emotional upsets may be reflected in the heart rate or sometimes in the total body weight Disorders of intelligence may be revealed by intelligence tests (though there is a large subjective element here as they require the active co operation of the subject)

Because of this need to depend so largely on the *symptoms it is much more difficult to assess the* value of psychotherapy than that of treatment for diseases of the body In the latter case it is easy to assume wrongly that some remedy has been the cause of improvement With psychotherapy this error may equally occur and there may also be the additional error of misjudging the degree of improvement

In spite of these difficulties it is sometimes possible to be sure that psychotherapy has been beneficial because it gives immediate results The man with a paralysed arm who by persuasion is made to use it is even more certainly relieved by psychotherapy than is the subject with meningococcal meningitis cured by sulphonamide If a man who is acutely anxious because he fears cancer is convinced that his fears are mistaken the immediate relief of his anxiety must be ascribed to psychotherapy not merely to a coincidental improvement In circumstances of this kind the value of the treatment can be assessed in each individual case just as the value of insulin can be assessed for the individual diabetic without taking into account its effect on other diabetics

Assessing the ultimate results of psychotherapy provides the problem of almost insuperable difficulty Large scale series with a prolonged follow up provide a most imperfect answer because psychotherapy is not a measurable form of treatment as are drugs X rays and surgery and it is not the same when given to one man as when given to another Similar reassuring words and explanation may be used when dealing with two people who are emotionally upset but the treatments are not identical because the problems are not identical Moreover the natural history of psychological disorder is inextricably bound up with the external influences to which men are subjected It is easy therefore to deduce that psychotherapy has been the cause of some distant improvement in the state of mind when the real cause may have been a change in these external influences On the other hand the difficulties of assessing the ultimate value of such organic remedies as leucotomy and electric convulsion therapy are less because they are measurable and can be given in the same degree or amount to a large series of patients In spite of the immense natural variations of the mental disorders for which they are given large scale controlled studies over many years can yield sound information as to their long term value But such remedies are not usually called psychotherapy

true at least in the short run The severity of all symptoms partly depends on the subject s state of mind and this state may be influenced by a bottle of medicine containing no active principles But it is another thing to suggest that the placebo can through its effect on the mind influence the course of an organic process Even if a *supposedly psycho somatic* disease is considered such as coronary artery disease (and the psychosomatic theory is for the moment accepted) it is hardly conceivable that the state of the coronary arteries could be improved by a *bottle of medicine* or by massage applied to the chest wall just because the patient has faith in them

In treating the acutely sick some specific or symp tomatic remedy is nearly always indicated Here therefore there is no need for placebos to alleviate symptoms since the placebo effect will automati cally be achieved by the specific or symptomatic remedy But in treating the chronically sick who are free of such symptoms as pain which can be relieved by symptomatic drugs measures to mini mize the symptoms would be most valuable Com mon symptoms of such patients are the general feelings of weakness tiredness and exhaustion

It may be accepted that sometimes a placebo can *temporarily relieve persistent symptoms* This is best seen in gross hysterics A patient with hysterical paralysis of an arm is told that he will be given a wonderful draught by mouth and a potent injection and that these will join together to form a healing *compound which will make his paralysed arm move* If water is then injected into his buttock and he drinks an effervescing mixture of valerian and asa foetida the result may occasionally be remarkable It is doubtful whether such deception is justified *The essential disorder is in no sense cured* and further gross hysterical symptoms will often recur which a repetition of the treatment does not remove No doubt the gross hysteric is often a *hopeless proposition* but such methods may make him worse rather than better

In so far as those with chronic organic diseases are temporarily helped by placebos the mechanism of relief is probably similar in principle to that of the gross hysteric The man with weakness and stiff ness of his arm following injury may believe that a bottle of coloured water in whose virtues he has faith improves his prowess But the result is that he depends not on his own efforts but on what others do for him In the long run he will probably be more disabled than he would have been had he *from the start been urged by constant effort to* try to improve the function of his damaged limb These considerations are particularly relevant to physiotherapy because the average man is more easily convinced that massage radiant heat or electricity directly applied to some lesion is the real means of recovery than that he should rely on a bottle of medicine

Theoretical arguments against the use of placebos of the kind advanced probably have little influence on those who regularly use them similar arguments have often been advanced in the past but immense quantities of placebos continue to be prescribed Many general practitioners say that on financial grounds alone they have to give patients their bottles of medicine if they do not the patients will go to other doctors who are more obliging But other general practitioners claim that they avoid placebos and retain their patients except the hopeless *minority whom no doctor wishes to* have on his list It is also argued that although a psychothera peutic session may sometimes be superior to a placebo in practice it is impossible to spend 15 minutes or more in talking to the individual patient *But if the psychotherapeutic session is* successful the patient will stop the regular visits in which he asks for repeat bottles of medicine thus in the long run saving the doctor s time a quarter of an hour spent now may save numerous spells of a few *minutes in the future Psychotherapeutic* sessions unfortunately are not always so successful

If placebos are used it can reasonably be urged that they should be cheap at least when the cost is being borne by the public purse There can be *no defence of prescribing expensive mixtures* of vitamins and elaborate proprietary tonics when the suggestive effect of a placebo can just as well be obtained by simple bottles of coloured water or evil mixtures of valerian or asafoetida

PSYCHOTHERAPY

Most patients are given psychotherapy *either de liberately* or incidentally Merely announcing the diagnosis often has a beneficial effect especially when it is less serious than was feared The state ment that an operation has been successful or that the prognosis is excellent is also *most reassuring* *Nevertheless* too much attention is apt to be de voted to the body and too little to the mind This is especially so when the patient has some obvious organic lesion the lesion is treated but the person behind it is often forgotten When on the other hand the patient is thought to be free of organic

and accept the risk of recurrence of their ulcers Only when a patient s ulcer is related to some such worry as the fear of cancer which can be relieved by reassurance is ordinary psychotherapy likely to help Moreover the overriding reason for giving this psychotherapy is to improve the state of mind and it is applicable to all men who are worried whether or not they also have ulcers even if it does not heal their ulcers it will make them feel better

It is too easily assumed that a knowledge of aetiology necessarily yields useful information about prevention and treatment Alkali or gastrectomy are excellent remedies for the subject with duodenal ulcer if they make him better even though the ulcer is psychosomatic The only objections to gastrectomy are that it is risky does not invariably prevent further ulceration and may be followed by troublesome sequelae If it had none of these disadvantages it would be the perfect remedy for duodenal ulcer however caused It would not put right the psychological disorder underlying the ulcer but that disorder is the proper field for psychotherapy

The value of psychotherapy in influencing the course of so called psychosomatic diseases is there fore small even in the particular case when the disease has been precipitated by emotional factors This does not mean that psychotherapy has no part to play in dealing with patients with these diseases They may be worried about the disease they may have various bodily symptoms directly due to their emotions which they wrongly ascribe to their disease or they may have unnecessarily turned themselves into invalids Psychotherapy here is similar to that given to sufferers from chronic and recurrent diseases which are not thought to be psychosomatic this matter will be dealt with below (p 51)

Patient with Emotionally-caused Somatic Symptoms

A high proportion of patients are free of significant organic disease and complain of emotionally caused somatic symptoms In addition they may have such mental symptoms as depression irritability sensa tions of tension and anxiety though they do not always mention them

The diagnosis and treatment of the patient with such symptoms cannot be sharply separated as they can with the subject of organic disease The actual process of discovering the cause of the symptoms can itself be therapeutic or can immediately lead to appropriate explanation and reassurance This is strikingly so when the patient wrongly believes that the symptoms are due to some grave disease

When the symptoms have been present for many years or always with little remission and are very numerous the possibilities of useful psychotherapy are small Nor can much be done when the symptoms are clearly related to some grave external disaster The hopeful situation arises when the symptoms are recent and have been precipitated by some comparatively trivial cause

When there is no obvious explanation of recent symptoms the first step is to find out what has precipitated the trouble Sometimes no definite cause can be found and the only conclusion is that the responsible factor is the patient s personality in conjunction with the general problems of existence Frequently there is a cause of which the patient is unwilling to speak In the ordinary circumstances of general practice it is possible if the doctor has the patience interest and time to pursue the matter to gain his confidence and persuade him to divulge his fears In the typical out patient department of a hospital this is impossible Patients will not reveal their innermost thoughts to a physician who has with him a secretary nurse and house physician with perhaps a crowd of students Many of those who work in hospitals take the view that they are exclusively concerned with the bodily state (or if specialists with some particular bit of the body) and that it is not their business to delve into their patients state of mind This attitude is deplorable implying that patients are not human beings with hopes and fears but aggregations of organs Every patient whose emotional state is relevant to the understanding of his symptoms should be seen pri vately at some stage of the proceedings Since it is impossible to be certain which these patients are in practice the best plan is to give them all a private interview If those in charge of out patient depart ments insisted on this course practical difficulties would disappear In non teaching hospitals there is nothing to stop the physician conducting the whole proceedings in private summoning a nurse only when he is examining women

At the private interview the patient should first be encouraged to describe his symptoms and to give his views as to their significance Sometimes he will be fully aware that they are bound up with his emotional state when he is worried he becomes aware of palpitation feelings of pressure on top of the head nausea and abdominal discomfort sweat ing from the armpits and trembling Frequently he will suspect that his symptoms are due to some dread disease which he may never mention because of his terror lest his suspicions be confirmed Lead ing questions should therefore be asked about such

The Acutely Sick Patient

As a rule psychotherapy for the acutely sick needs to be only of the most obvious and superficial kind Anyone who is ill naturally wishes to know what is the matter with him how long the illness is going to last and whether he will make a complete recovery His relatives may be equally or more anxious and ask for similar information and when the patient is comatose or so ill as to be unaware of what is happening they alone will be interested in this matter When the outlook is good the decision as to what to tell is simple the unvarnished truth is then the most reassuring of all kinds of psychotherapy Whether or not the patient asks about his condition and his future this reassuring statement should always be given and may usefully be repeated whenever he is seen When the outlook is uncertain as after a cardiac infarct it is not so easy to know what to say Probably the right policy is to say that satisfactory progress is being maintained and that there is every hope of complete recovery To tell him that he may have another attack any time that he may suddenly die or may be left incapacitated would be cruel and serve no useful purpose though the possibility of these disasters should no doubt be imparted to the relatives On the other hand he should perhaps be informed that further attacks in the distant future are possible though unlikely for many years

The main object therefore of psychotherapy for the acutely sick person is not the important one of preventing his death but the subsidiary one of lessening the distress caused by his illness Apart from those with such acute illness as strokes and poliomyelitis which may be followed by permanent organic sequelae and are best considered along with the chronic diseases it matters comparatively little if psychotherapy is omitted altogether Even if the doctor is wrongly gloomy painting the blackest picture of the outlook as soon as recovery takes place his words are forgotten in the prevailing joy On the other hand if a satisfactory outcome is predicted but the patient dies the soothing words which had been poured forth will give no relief to the relatives

Another object in giving psychotherapy to the acutely sick is sometimes the prevention of psychiatric sequelae This is relevant to the diseases which may cause organic sequelae and particularly to those such as rheumatic fever and cardiac infarcts, which may cause cardiac sequelae Everyone knows that rheumatic fever may be followed by cardiac damage The convalescent from this disease who has escaped such damage may become aware of palpitation sighing respiration left mammary pain and other emotional somatic symptoms and takes it for granted that they are due to his damaged heart. Reassurance about these symptoms along the lines described below (p 49) can be most beneficial

Patient with a 'Psychosomatic Disease'

It was previously concluded (p 3) that the significance of psychological factors in the aetiology of organic diseases has been greatly exaggerated by some in recent years The evidence that coronary artery disease and other arteriosclerotic conditions and rheumatoid arthritis are often psychosomatic is slender Although psychological factors are sometimes important in the development of peptic ulcer thyrotoxicosis certain skin diseases and other conditions these disorders cannot always be explained on psychological grounds Indeed no organic disease with the possible exception of venereal diseases can baldly be called 'psychosomatic' for this implies that the development of the disease can wholly be explained by psychological factors The most that can be said is that such factors are in some cases of some relevance

When emotional factors seem to have been responsible for organic disease it does not follow that useful treatment can be given It is then already too late to prevent the disease developing so the most that can be hoped is that the future course of the process will be favourably influenced This is particularly relevant to such relapsing conditions as duodenal ulcer and ulcerative colitis If a man who is going bankrupt is suffering much pain from his duodenal ulcer or a widow whose only son is a drunkard and a wastrel is having haematemeses action is clearly desirable The doctor can do nothing to improve these situations and soothing words are hardly likely to help When the chief factor in causing the ulcer is thought to be the patient's highly nervous temperament so that he constantly worries about trivialities no psychotherapy will make him calm and phlegmatic Even when a man's emotional state could be improved by his giving up some worrying though inessential activity it is questionable whether the right course is always to advise him to do so Although emotional tension may thereby be lessened a sense of depression or of inferiority at having abandoned the fight may take its place Many men given this sort of advice would refuse it feeling that they would rather continue in their usual practices which mean so much to them

bodily disease and whatever is said they conclude that because the doctor states that they are free of bodily disease he must mean that the symptoms are imaginary" Such patients are those of hysterical temper with symptoms which have a purpose The victim of a head injury who hopes to get compensation may know that his headache and other troubles are due to a fractured skull and bruising of his brain The attempt to persuade him that his brain suffered no more than temporary damage will probably fail completely In so far as patients have a conscious or unconscious desire to perpetuate their symptoms they provide a formidable therapeutic problem This can be overcome only by a radical change in their attitude which can rarely be achieved Ordinary measures of reassurance explanation and encouragement are usually futile As a rule only by so changing the patient s circumstances that he no longer needs his symptoms will improvement occur Such a change is in most cases impracticable and if it is practicable it can hardly be called psychotherapy One situation in which there is a hope of success is the compensation case when the legal procedures are finished and the amount of compensation settled the need for symptoms disappears

Patient with Chronic or Recurrent Organic Disease

The most obvious psychotherapy in managing the patient with chronic or recurrent organic disease is a factual statement of the nature of the process the outlook and the treatment needed In general it is wise and kind to say nothing of the possibility of some distant or unlikely disaster It would be cruel to tell someone who has had a stroke that another stroke may later make him worse or kill him though as it is widely known by the public that strokes recur perhaps the possibility of further trouble should be mentioned with the assurance that this is unlikely for a long time On the other hand when it is certain that someone is going to be permanently disabled or is faced by a long spell of illness to pretend that he will recover completely or that his illness will be brief is a false kindness Sooner or later he must know the truth and better sooner rather than later This is applicable to those whose eyes are so badly damaged or diseased that blindness is inevitable or to those whose spinal cords are so damaged that they will never walk again It is best that they should face up to the unpleasant realities of the situation by learning Braille or by so adjusting their circumstances that they can work and play from a wheeled chair

Perhaps a factual statement about the outlook is most likely to be forgotten when a patient is given highly successful treatment which has to be continued indefinitely The subject of pernicious anaemia can be kept well until the end of his life But this fact (which is so obvious to the physician as initially he observes the reticulocyte response and later he notes the normal haemoglobin figure) may not be imparted to the patient He knows that he has pernicious anaemia which gives a most discouraging impression and that he has to attend regularly for injections Although he no doubt realizes that he is much better he may still continue to think of himself as a sufferer from pernicious anaemia He should be told from the start that he will be free from anaemia for the rest of his life provided he has his monthly injections and that if he ever feels unwell this can have no possible connexion with his blood The subject of myxoedema should be similarly treated

A difficult situation arises when the nature of the disease is obscure When it seems likely that the patient has some serious disorder and when the lapse of time or investigations may provide a definite answer only a tentative opinion should be given Frequently it is possible to conclude that the condition though obscure must be benign as in cases of long standing pains in the back and limbs indefinite varieties of headache which have gone on for years or many vague kinds of chronic dyspepsia Symptoms of this kind may sometimes be due to emotional upsets but often they can be attributed only to some minor pathological process or some recurrent functional" upset the nature of which is unknown (*see* p 7) Those with such symptoms are often told that they have rheumatism fibrositis "neuritis gastritis colitis or other similar entities and if their medical advisers *do not make such diagnoses they often make them* themselves Indeed patients habitually complain not of pain but of rheumatism or neuritis and much discussion may be needed before the precise nature of their symptoms becomes clear

It is far from easy to know what should be said to patients of this kind No doubt such meaningless labels as rheumatism or fibrositis are harmless though alarming diagnoses which encourage patients in the belief that they are invalids such as blood pressure or myocarditis should never be used Perhaps in general the best policy is to speak along the following lines I can first give you a categorical guarantee that you cannot be suffering from any serious disease The main reason for saying this is that you have had your symptoms for very many years and yet are still able to go about your usual

disorders as heart disease blood pressure venereal disease tuberculosis insanity and in particular cancer—the disease about which nearly everyone feels some apprehension and many have an all pervading dread Alternatively by private discussion the patient may reveal some circumstance which he thinks disgraceful such as the cruelty drunkenness or unfaithfulness of a spouse the pregnancy of an unmarried daughter or the criminal activities of a son

A promising discovery from the therapeutic angle is the *unjustified fear of grave disease* A man is reaching the age at which his father suddenly died from a heart attack He knows that heart disease runs in families and that his father was well up to the moment of his death He develops palpitation aching in the left side of the chest difficulty in filling his lungs giddiness and other symptoms which confirm his suspicions that the state of his heart must be very bad He gets into a vicious circle of worry the worse his symptoms the more does he worry about them and the more he worries the worse are his symptoms A confident statement that these symptoms are never due to disease of the heart but are just the feelings which people get when they are worried may remove the burden from his mind completely and abolish them for ever Similarly the subject with flushings full feelings in the head and giddiness may take it for granted that he is suffering from blood pressure and be afraid that he is going to have a stroke (He may indeed have the presenting complaint of blood pressure and a lot of discussion may be required before the actual nature of his symptoms is determined) If the blood presure is normal a thorough reassurance is easily given but if it is above average the doctor can fall into the same error as the patient and assume that the symptoms are due to this In fact symptoms of this kind are not *caused* by a raised blood pressure (though both the symptoms and a rise of blood pressure may be caused by the same emotional upset) If the patient already knows that his blood pressure is raised he should be given an unequivocal promise that his symptoms have nothing to do with this and he should be assured that the pressure is no higher than that of numerous other people of his age If he only fears that his blood pressure is raised it is probably best to say that it is normal when the readings are only a little above average When the readings are very high perhaps the best plan i to say that there is some elevation of blood pressure but that the symptoms have no connexion with this In any case the exact figures should never be disclosed

If the patient fears cancer an unequivocal promise that this is absent cannot in truth be given since it is always possible that he may have some deep seated growth The patient moreover may be aware that it is impossible to exclude cancer But if the symptoms have been present for a long time he can rightly be promised that they cannot be due to cancer since if this disease had been present when they first developed he would have been dead long ago He can also be assured that his symptoms are not those of cancer but are just those of a man who is worried and depressed

A difficult situation arises when the patient has previously been given some such diagnosis as heart strain myocarditis or visceroptosis to which he attributes his symptoms It is then necessary to say that no evidence of any such condition can be found which must imply that a previous medical adviser had been mistaken But by a thorough explanation as to how the symptoms are bound up with the emotional state it may be hoped that even the patient who has been convinced for years that his heart is diseased may be given some insight into his condition and complain less in future

When the precipitating cause of the trouble is some external disaster which must be borne the patient may make himself worse by worrying about his symptoms which consequently become more noticeable and in turn increase his anxiety a vicious circle being established The man in financial difficulties may develop insomnia weakness exhaustion palpitation and indigestion and therefore fears that his health is failing or that he is going insane If he is given insight into his symptoms they may become less troublesome and less alarming It may also be possible to modify the patient s attitude to some unpleasant situation making it seem not so bad as he thought

Psychotherapy of this kind is constantly given by relatives or friends The mother reassures the child about his difficulties at school and the wife reassures the husband about his troubles at work But many lonely people have no one to whom they can turn when in trouble and their doctor may be of great help by acting as a friend rather than as a physician Moreover the doctor s position gives his words an influence out of all proportion to their intrinsic merits

In dealing with patients with emotional bodily symptoms the impression should never be given that they are imaginary On the contrary the doctor should always make it clear that he fully appreciates how real and trying they are He can perhaps describe how he himself has at times had similar symptoms and how unpleasant he found them

A proportion of patients refuse to accept that their symptoms are due to their emotions not to

which doesn t distress you and eat anything you like which doesn t upset you is a great encouragement to overcoming disability Even if it were in fact true that activity would be likely to shorten the life of some man with a chronic disease it may still be the best policy to advocate such activity for a good short life is better than a miserable long one

Psychotherapy of this kind is of particular im portance when the patient s treatment depends largely on himself The diabetic provides a good example He should be told that provided he fol lows his simple rules he can be guaranteed the full return of his weight and strength and the dis appearance of his symptoms and that he will be able to take part in nearly all activities He should be encouraged to give his own insulin from the start—preferably the morning after the decision has been made that he needs it—and shown how to adjust his dose Indeed he should be imbued with the idea that he is to manage his own treatment the doctor merely advising him about occasional difficulties In this way it can be hoped that the diabetic will take pride in the fact that he is as good as or better than other men and will never use his disease as an excuse for his failings or as a means of getting his own way

By urging the chronic sick to overcome their dis ability it is sometimes possible to influence an organic process If those with chronic arthritis are left alone they may develop contractures and mus cular wasting of such degree as to become helpless But if spurred on by their doctors perhaps with the aid of splints and the activities of physiotherapists their joints may be kept straight and their muscles strong The essence of the doctor s task here is to put the onus of recovery upon the patient and pre existing ideas of the necessity of massage and other passive varieties of physiotherapy (which must give the impression that the cure depends on the activi ties of others) should be vigorously suppressed Overcoming the disability due to obesity provides a more striking example All the patient s instincts are opposed to the only effective course—to starve himself of fat and carbohydrate foods Although nothing could be more organic" than a thick coat of fat nothing could be more certain than that the removal of fat is a psychological problem If there fore a patient is so fat that the gains of losing weight appear to outweigh the losses of dieting no effort should be spared in convincing him that this is so The obvious disadvantages of his state and his poor expectation of life may be stressed and an unequivocal promise should be given of the harmlessness of losing weight

Perhaps this sort of encouragement provides the greatest triumphs of simple psychotherapy and it is particuarly applicable to those with organic dis ease The gross hysteric with his extravagant mani festations provides a difficult or insoluble thera peutic problem the subject with chronic disease who has unnecessarily made himself into an invalid provides a much more hopeful prospect If he can only be shown how much better it is to overcome rather than give way to a disease there is every likelihood of achieving a measure of success and of enabling him to lead a more satisfying life

Patient with Malignant or Progressively fatal Disease

The decision what to say to the patient whose con dition is hopeless is difficult If the doctor tells frank lies promising that recovery is just round the corner he may raise hopes temporarily but inevitably they will soon be dashed On the other hand if he tells the brutal truth he will make the unfortunate patient even more depressed than he is already

A simple and widely used method of dealing with this problem is to shelve it and say nothing at all about the future The patient is merely asked how he feels is congratulated if he says he is a little better or if he has some symptom is given a suitable preparation to relieve it This method is often suc cessful in that the patient accepts this day to day attention and never inquires about returning to work or about getting up again until he relapses into the final stuporose state in which he is mercifully incapable of thinking about the future

In particular it is the usual custom in Britain to avoid the word cancer when talking to patients with this disease Instead they are told they have an ulcer an obstruction or perhaps a tumour Often it seems highly probable that the patient well knows what is the matter with him but never mentions his suspicions to his doctor There is therefore a double game of make believe The doc tor knows that the patient knows what is wrong but both behave as if the other is ignorant

This shelving of the problem is oft n the kindest and best as well as the simplest way of dealing with it especially when the outlook is without doubt hopeless On the other hand when there is a good chance of eradicating the mischief perhaps the best policy is to be more outspoken The woman who is told that she should have her breast removed probably knows or fears that she has cancer and may be fully aware that cancer often breaks out

affairs no serious disease ever behaves in this way My examination also confirms that there is nothing seriously the matter but unfortunately it is not possible to say exactly why you are liable to pains and other symptoms Do not think there is anything unusual in this You must be well aware that nearly everyone sometimes has a headache yet only a tiny minority of headaches can be explained Most people have backache and bellyache at times and the reasons for these symptoms too are nearly always unknown or obscure You are unusual only in that you have complaints of this kind more often than does the average person Medical science has made great advances but we still know very little about the rheumatic complaints If you can be con vinced that there is nothing seriously the matter you will at least stop being worried about your symptoms and if you do that I am sure that you won t notice them nearly as much as you have done Otherwise I am afraid there is little we can do if your complaints had been curable they would have been cured long ago If the pain is bad there is no objection to your taking aspirins or if your indi gestion is bad you can use alkaline tablets if they help As regards diet I can only suggest you are guided by your own experience Some patients at least seem to be helped by a talk along these lines

Patient with Emotional Symptoms Due to Bodily Disease

People with a chronic or recurrent disease are usually worried about it and in consequence are apt to develop somatic symptoms of emotional origin These symptoms moreover particularly arise from the affected region The subject of rheumatic heart disease often complains of left mammary pain palpitation difficulty in breathing and giddiness the consumptive may have vague pains all over his chest and the diabetic who knows that diabetics develop gangrene may have aches and pains in his legs These symptoms in turn be come a source of anxiety adding conviction to the fear that the disease is very serious a vicious circle being established

In treating patients with these diseases therefore an inquiry should always be made about symptoms of this kind for patients may refrain from mention ing them because of the fear that they are of ill omen Confident reassurance should then be given and it should be explained which symptoms can be ascribed directly to the disease and which to the emotional upset associated with the disease Psycho therapy is probably more effective for such patients than for those with emotional bodily symptoms who are free of organic disease The latter are psycho logically unstable and though they can be helped can hardly be cured the former may be of sound personality The hitherto stable man who is told that he has heart disease is apt to suffer profou d psychological trauma he is only too anxious to be reassured and will usually accept gladly the con fident statement that his palpitation aching in the chest and other symptoms are due not to his heart but to his natural anxiety There is every hope that thereafter he will cease to be troubled by symptoms of this kind

Minimizing Disability People vary infinitely in the degree to which they are disabled by any given lesion This is partly related to the extent to which they develop emotional symptoms and when they have such symptoms their disability can be mini mized by reassurance Quite apart from this people have greatly differing attitudes towards their dis eases One man with advanced rheumatoid arthritis will succeed in carrying on his work as a skilled craftsman another will stop working permanently and spend the rest of his days as an unhappy invalid One woman who has had a complete tran section of the spinal cord will live a miserable bed ridden existence another will move to a bungalow teach herself how to use a wheeled chair arrange her household to suit her needs do all the family shopping cooking and sewing and enjoy a happy life basking in the admiration of all who know her

The patient s attitude is to a large extent outside the doctor s control In general those of good per sonality minimize their disability those of weak personality exaggerate it But by encouragement and enthusiasm it is often possible to inspire people to overcome their trouble As regards the blinded and the maimed everyone agrees that the doctor should endeavour to do this but many of the ordinary chronic sick are encouraged to be semi invalids for therapeutic reasons Those with high blood pressure well compensated heart lesions or rheumatoid arthritis may be told that numerous activities are forbidden Even if the doctor does not take this attitude the relatives may do so Some people are actually compelled to consider them selves as invalids especially when they are recruits for the services or are endeavouring to obtain employment On account of albuminuria flat feet or varicose veins a man capable of being a valuable soldier may be decreed unfit for any form of mili tary service

There is rarely evidence to support permanent restriction of activity greater than that dictated by the symptoms In general a chronically sick person who is not immediately upset by some activity or article of diet will not be upset in the long run The very statement You can do anything you like

CHAPTER 6

Prevention of Disease

JOHN W TODD

THAT prevention is better than cure is a truism In recent years the medical profession has often been accused of taking too much interest in established disease and too little interest in prevention and in discovering disease at an early curable stage The hope is expressed that in future doctors will spend less of their time among the sick and more among the healthy whom they will examine regularly and advise on their habits of living We are exhorted to convert the National Health Service from what it is at present an ill health service into a true *health* service

Infections

The means of preventing infection can be put under two heads first stopping the organisms from reaching people (as by clean water supplies or by rendering the sputum of consumptives non infective) and second making people insusceptible (by vaccination or by non specific methods of raising the powers of resistance')

The air borne infections are overwhelmingly the most important in the Western countries Nearly everyone has one or more common colds each year often associated with acute bronchitis Chronic bronchitis is extremely common (though other factors as well as infection seem to be responsible for this syndrome) Influenza in its severe forms may decimate the population and the minor epidemics occurring each year cause much sickness and many deaths in the old Pneumonia still kills thousands in spite of the anti bacterial drugs Pulmonary tuberculosis remains a not uncommon cause of prolonged illness and death Is it possible to do more than we are doing by further application of these methods of prevention?

Whether we can make appreciable progress by trying to prevent the spread of the acute common and highly infectious conditions is most doubtful Epidemics appear and spread freely throughout the susceptible population Such individual measures as gargling nose washing and the wearing of masks in public have been advocated but probably have little effect and as regards masks are most distasteful People are also urged to stay in bed for a few days as soon as a cold or flu begin in order to save others from infection If this were a universal practice it is by no means certain that there would be much fall in the incidence of these conditions but there is no possibility that it ever will be a universal practice Doctors notoriously are worse than the general public in carrying on with their work when they have colds or flu Children with such specific fevers as measles and mumps are isolated when the diagnosis is made but this probably has no appreciable effect in the long run sooner or later nearly everyone acquires these infections

Other formidable factors in mitigating efforts to spread infection are the symptomless carrier of various organisms and the subject who has had a subclinical attack of a disease Indeed so far from increasing our efforts to stop these common acute infections from spreading we would be well advised to get rid of some of the futile practices which have no effect to this end but cause much dislocation In particular the quarantine rules which though often ignored still cause numerous children to miss long periods at school because their brothers and sisters have measles mumps rubella and chickenpox could with general profit be allowed to lapse

These considerations are not applicable to pulmonary tuberculosis Those who spread the organisms may remain infective for years and they form only a very small proportion of the population An important means of fighting this disease is to seek out and isolate or render non infective the persistently infective minority

In the prevention of most air borne infections therefore we must look not to hindering their spread but to making people insusceptible The specific method of doing this—immunization—is of great value for smallpox and diphtheria (both of which are nearly extinct in Britain) and probably of considerable value for whooping cough and

again later The true statement that she has cancer but in a comparatively innocent form with an excellent chance of cure may be less worrying than ignorance

In treating the malignant or hopeless case there is then little place for anything which can be called 'psychotherapy Few sound generalizations can be made and the action in each individual case should be decided on its merits No subtle theories or psycho analytical sessions but common sense in conjunction with a kindly and encouraging manner are needed here

EARLY DIAGNOSIS AND TREATMENT

If diseases cannot be prevented the next best means of dealing with them it is often said is to discover them at an early curable stage But since many conditions are uninfluenced or hardly influenced by treatment the question of their early or late discovery is unimportant Among them are the virus infections (except in so far as they give rise to treatable complications) many degenerative diseases disseminated sclerosis and other chronic diseases of the nervous system many congenital abnormalities and some of the chronic rheumatic conditions Other diseases can be just as well treated when they have been present for a long time as when they are early This is true of a high proportion of chronic innocent lesions susceptible to surgery such as uterine fibroids and most other benign tumours prolapsed uterus piles hallux valgus and other orthopaedic abnormalities and up to a point herniae and varicose veins Moreover when they are really "early they should not in general be treated A hysterectomy in a menopausal woman with a large mass of fibroids and excessive uterine haemorrhage can be one of the best of all operations to perform the same operation or even a myomectomy on a young woman with no symptoms because a small fibroid has been discovered by accident would be folly Radical cure of an indirect inguinal hernia which is large enough to cause discomfort is admirable repairing a doubtful bulge which is doing no harm is misguided And when conditions of this kind are early the question whether they are causing any symptoms arises The young woman with early varicose veins may complain of aching in the legs fatigue and other symptoms which she attributes to the veins but whether this is so is doubtful except in so far as the veins are a source of worry and embarrassment to her Certain chronic medical conditions such as myxoedema and diabetes can be treated nearly as successfully when they have been present for a long time as for a short time the same is true up to a point of leukaemia lymphosarcoma lymphadenoma and other varieties of malignant disease which are widespread from the start

Perhaps the diseases in which prognosis is most strikingly influenced by the stage when treatment is first given are the potentially fatal acute infections susceptible to specific drugs and certain acute abdominal disasters The subject with malignant tertian malaria meningococcal meningitis staphylococcal septicaemia acute intestinal obstruction or ruptured ectopic gestation who has been ill for days or in the case of some of them for hours stands a far poorer chance of recovery than if treatment had been given when symptoms first developed But those who advocate early diagnosis and treatment in general terms probably have in mind not these hyperacute conditions but the more chronic diseases which the patient is apt to neglect In Britain most people who are seized with one of these acute disasters summon medical advice immediately Delay in instituting treatment is usually due to the doctor s delay in visiting the patient to mistaken diagnosis or to difficulty in arranging admission to hospital Health propaganda to the public will have little effect in improving this situation

Among the chronic conditions whose curability is thought to depend particularly on their stage of development are most kinds of malignant disease and tuberculosis Indeed other things being equal the smaller and earlier is a malignant lesion the better is the chance of cure But the age of the process is not the only factor which determines the outcome In general a more important factor is the degree of malignancy This is well illustrated by the series of cases showing that the longer the disease has been present the better is the outcome Sometimes the process is so comparatively benign as in carcinoma of the breast in old women that even without treatment the patient dies several years later from an unrelated condition On the other hand some cancers metastasize almost from the start many of the victims of carcinoma of the lung present with symptoms due to secondary deposits

Another factor which can profoundly influence the outcome is the site of the disease it may be possible to remove a growth from one site but impossible from another A peripheral growth in the lung is suitable for pneumonectomy (provided there are no secondary deposits) a growth of similar size and malignancy in the hilum is usually hopeless A glioma in the left temporal lobe may be technically operable but the operation would leave the patient a helpless wreck a similar growth in a cerebellar lobe will probably be suitable for radical excision In practice too the site of the disease often determines whether the patient seeks medical advice Superficial growths such as those of the breast mouth and skin cause symptoms when they are very small deep-seated growths such as of the pancreas and stomach can become large before their subjects are aware of them The site within an individual organ may also be important Stomach growths starting in the pyloric region give rise to symptoms much sooner than do similar growths starting higher in the body

Many people fail to take advice when they first develop symptoms of malignant disease Breasts re

tuberculosis but of small or doubtful value in other circumstances Perhaps effective vaccines for influenza and the common cold will some day be produced though in view of the enormous efforts already made we cannot be confident

There are often said to be non specific measures of raising the general bodily resistance to all infections These measures are included under the general heading of good hygiene or healthy habits of living Among them are daily cold baths regular exercise fresh air adequate sleep good food and a calm unhurried existence As these measures cannot be defined in precise terms and as they have not been subjected to the critical analysis of large scale controlled studies it is impossible to know whether they are at all effective That they are not strikingly so is clear since many who adopt them are not immune from colds and other infections On the other hand the incidence of certain infections notably tuberculosis is much higher among the poor than the rich which suggests that the habits of living may have some influence A good deal of this increased incidence among the poor can reasonably be ascribed to their increased opportunity of infection This is particularly so with infants and the difference between rich and poor is most marked in their case

Even if infections could be prevented by healthy habits of living this is of little practical importance Most people are fully aware that fresh air adequate sleep regular exercise and the other measures are said to be healthful but they freely choose to live in ways which they know are unhealthy The upper classes in Britain send their sons to boarding schools where they have no choice but to go to bed early have daily cold baths take plenty of exercise and eat the plainest and most wholesome" food After leaving school they soon adopt less austere habits It is also of little importance in the practice of medicine that the incidence of infection would be lowered if the living standards of the poor could be raised medical men have no power to raise them (To raise living standards is of course desirable irrespective of its effect on the vital statistics)

A group of infections which are easily preventible are the venereal diseases Everyone knows that by the simple expedient of refraining from sexual intercourse he can virtually be guaranteed immunity The fact that so many do not do so illustrates the futility of some of the popular talk about preventible diseases In so far as men who have the ability and knowledge to prevent themselves from acquiring a disease nevertheless continue to acquire it for practical purposes it is not preventible

Degenerative and Malignant Disease

In the Western countries the main causes of death are the degenerative conditions associated with arterial disease and malignant disease Environmental factors have been identified in the aetiology of a few varieties of malignant disease Examples are skin cancer occurring in those exposed to certain irritants and bronchial carcinoma which is far commoner among cigarette smokers than among non smokers In future environmental factors responsible for other malignant growths will no doubt be discovered but at present the aetiology of all the common malignant growths except bronchial carcinoma is obscure Clearly therefore we can do very little to prevent cancer In preventing bronchial carcinoma there is the similar difficulty already noted in connexion with the venereal diseases The public has been widely informed in recent years that this disease usually occurs in heavy cigarette smokers but tobacco consumption continues to increase It seems unlikely that an intensive propaganda campaign such as has been advocated would cause a dramatic reduction in smoking An important hindrance to such propaganda is that many years of heavy smoking precede the disease men in their early twenties cannot easily be persuaded to worry about what will happen to them in their fifties and sixties Probably the best hope is to discourage the young from ever starting to smoke and in Britain at present a valuable additional weapon is the high cost of tobacco

We know little about the aetiology of the conditions associated with chronic arterial disease They have been attributed on very little evidence to anxiety overwork or the stress and strain of modern life but their tendency to run in families and their fairly similar incidence throughout the whole population suggests that inborn factors are more important than environmental Even if they are sometimes due to stress and strain they are not for practical purposes preventible Very few men can change their whole circumstances of life and none can change their temperaments (which may make them unduly conscious of strain) These diseases have also been attributed in part to a diet high in animal fat over many years There is far less likelihood that men will live on a diet nearly free of animal fat throughout youth and middle age to avoid coronary artery disease than they will refrain from cigarette smoking to avoid lung cancer and chronic bronchitis

formidable procedure of thoracotomy may be performed after which a biopsy is taken or if it seems likely that a carcinoma is present pneumonectomy is carried out If the shadow suggests tuberculosis and there is no sputum the subject may be treated as if he has this disease or alternatively he may merely be advised to have repeated radiographs

If in fact, the subject has a malignant growth all this will usually have been well worth while and frequently no doubt a life will be saved which otherwise would have been lost But even here nothing may have been gained because the lesion although so early has already metastasized If the subject has in fact a tuberculous lesion which is going to progress he will also gain But if he has a benign lesion or a tuberculous lesion which will resolve spontaneously a great deal will be lost by starting along the road which begins with routine examination The worst result is some such mutilating operation as radical mastectomy hysterectomy pneumonectomy or perineal excision of the rectum How often this happens it is impossible to say because the error is rarely found out The next worst result is that the subject is unnecessarily made into an invalid for some months or a year or two because of a non tuberculous lesion or of a tuberculous lesion which would have resolved spontaneously The best result is that the subject and his relatives are given a period of anxiety while the deliberations and investigations are carried out. When there is a shadow suspicious of pulmonary tuberculosis this period of anxiety may last months while further radiographs are taken

The value of routine medical examination in discovering malignant disease tuberculosis and other conditions whose curability declines if they remain untreated is often questioned because of the great effort and expense required to bring to light a small number of such lesions But the positive disadvantages of this procedure in causing unnecessary anxiety and invalidism and worst of all unnecessary mutilating operations are not so often stressed Moreover although clinical examination and chest radiography are benign procedures barium meal or enema radiography sigmoidoscopy and vaginal examination by speculum are not Even if there were enough clinicians radiologists and X ray equipment to make these examinations practicable for the entire middle aged population some 3 or 4 times annually it may well be doubted whether many people would continue to attend regularly

In practice the conditions most often discovered by routine clinical examination are various benign defects of the existence of which the subjects are often aware already Probably the commonest is dental caries Others are obesity varicose veins such orthopaedic abnormalities as scoliosis pes planus and hallux valgus raised blood pressure heart murmurs and albuminuria But whether treatment should be advised or if advised would be accepted is another matter No doubt the obese would be better off if they could be persuaded to starve away their excess fat But as a high proportion of obese people will not lose a great deal of weight and maintain the reduction when they seek medical advice because of their obesity very few are likely to do this after routine examination There are good grounds too for treating dental caries though for cosmetic reasons and to avoid toothache and false teeth in the future rather than for reasons of health The widespread neglect of dental caries can be attributed to laziness and indifference fear of the dentist s drill and the expense of dental treatment (though in Britain this is no longer a factor in children and a small one in adults) Perhaps the doctor could persuade some people to adopt a more sensible view point about their teeth but the routine examination of the mouth of followed by an argument with every patient is a most tedious method of dealing with this problem education and propaganda are surely the means to employ

Most of those with hallux valgus pes planus and other orthopaedic abnormalities have few or no symptoms and whether treatment should be advised for them is most doubtful In general the subjects with these conditions who require treatment are those with symptoms—and perhaps not all of them Routine medical examination is not necessary to deal with them effectively The same is true of most other chronic abnormalities from varicose veins to herniae from fibromas of the skin to pendulous breasts for those who find them troublesome and are willing to have operations for their cure will mostly seek advice of their own free will

At least one benign condition—namely anaemia—which is sometimes discovered on routine examination in subjects without obvious symptoms certainly should be treated Perhaps it develops so insidiously that the subject does not realize her condition has deteriorated or she may ascribe her malaise to the change or some other familiar bogey Only when the anaemia has been cured may she realize that previously she did not feel well

Not only are the fruits of routine examination meagre It also carries the risk of bringing to light abnormalities whose presence would better remain undetected This is often true of hypertension heart murmurs and albuminuria Many people who are free of symptoms before they are aware that they have such conditions develop anxiety symptoms when told of their existence and live unhappily thereafter

placed by an ulcerating mass of growth or large malignant ulcers of the mouth or tongue which their possessors know have been present for a long time are sometimes seen Ignorance may account for some of the failure to report very small growths but the continued refusal to seek medical advice is largely due to fear Since the treatment of these superficial growths is comparatively satisfactory they seem suitable subjects for propaganda urging the public to seek early medical advice An advertising campaign pointing out that in the middle aged and elderly every sore on the mouth or tongue which does not quickly heal any lump in a breast and vaginal discharge of irregular haemorrhage may be due to cancer and that the chances of cure are good might induce some people with such symptoms to see their doctors Similar propaganda relating to the two commonest cancers of men—carcinoma of the lung and stomach—would probably have a negli gible effect because when the symptoms first occur the situation is often already hopeless

Other things being equal the earlier progressive tuberculosis is treated the better But again another factor may have a more important effect on the outcome namely the natural severity of the pro cess Most people are infected by tuberculosis which heals spontaneously and of those with advancing lesions the rate of advance varies infinitely Old men are discovered who have clearly had gross pulmon ary tuberculosis for many years which has had no ill effect on them than to cause persistent cough and sputum others have a rapid pneumonic or miliary process which if untreated is soon fatal There is here another more important reason than the wel fare of the individual for discovering open tuber culosis—the infective risk to others A patient with advanced disease may be incurable but if he can be prevented from spreading his organisms others will be prevented from acquiring the disease

Only fairly small benefits therefore are likely from efforts to ensure early diagnosis and treatment even of malignant disease and tuberculosis With most other chronic conditions the benefits are smaller or non existent

Routine Medical Examination

This has been widely recommended as a means of discovering lesions at an early curable stage and to encourage good habits of living and general fit ness It is already employed for school children and for candidates for many jobs in civilian life and for the services (though not so much for the individual s sake as to keep away unfit men who may be a lia bility) No attempt has been made yet to encourage it for the general population of Britain though indi viduals sometimes ask their doctors for a general check up In America this is done on a wider scale often with an extensive series of investigations

Routine medical examination has no relevance to diseases with an acute onset except when a chronic condition is found likely to precipitate some acute process Without doubt the commonest of such con ditions is a high blood pressure If a middle aged symptomless woman is found to have a blood pressure of 210/110 it is a fair deduction that she will be unduly liable to cerebral haemorrhage But to inform her of her high blood pressure and of the hazards she is running and to put her on treat ment (which must go on indefinitely) by the ganglion blocking agents with their inevitable side effects would be mistaken There are excellent grounds indeed for not telling her anything about her blood pressure and she should certainly not be told the exact figure The discovery by routine examination of a lesion needing treatment of which the patient is ignorant is also unusual for the first manifestations of a high proportion of chronic dis eases are symptoms not physical signs In general therefore this method achieves results only with those people who do not seek medical advice when they feel unwell If they will not do that are they likely to see their doctor as a matter of routine?

There are nevertheless a few conditions in which early treatment is important which might be dis covered by clinical examination before symptoms develop Examples are small lumps or ulcers sug gesting carcinomas of the breast cervix uteri and rectum By special investigations other conditions would be found such as carcinoma of the colon by sigmoidoscopy a filling defect suggesting car cinoma of the stomach by barium meal radio graphy and shadows suggesting tuberculosis or bronchial carcinoma by chest radiography Pre cancerous lesions might also be found as in the cervix uteri by taking scrapings and examining them microscopically

But the very early lesions discovered in these ways do not provide a simple problem because there is often doubt as to their significance If the lesion is superficial the matter can be pursued by taking a piece of it for biopsy The pathologist may then be able to give an unequivocal answer that the tissue is malignant but often the doubt will remain or he may express the opinion that the lesion is pre cancerous Nor should it be forgotten that patholo gists can err though their mistakes are not so easily found out as are the mistakes of clinicians When a shadow suggesting carcinoma is found on a chest radiograph further methods of study such as bronchoscopy bronchography and sputum exam ination may sometimes yield definite information but often they do not If there is still doubt the

disorders of the body diminish men s happiness very little People who have lost single limbs or have flat feet herniae or a host of other innocent conditions seem to be little if any less happy than the average of mankind To some people a trivial complaint may even be a welcome friend by providing a convincing excuse for evading responsibilities and a means of gaining attention and sympathy As medical men we can unfortunately do very little in giving people equable temperaments financial security interesting occupations houses of their own loving wives children who are a credit to them and the other factors which enable them to live happily

THE INDIVIDUAL DOCTOR'S PART IN PREVENTING DISEASE

The above considerations suggest that whatever the possibilities of preventive medicine they are only to a small extent the concern of the individual practitioner dealing with his own patients The provision to all of water and food free of pathogenic organisms the destruction of disease carrying insects and the prevention of industrial diseases are not in the main medical problems though they may require the services of certain medical specialists The raising of the standard of living and the prevention of atmospheric pollution by which means tuberculosis chronic bronchitis and some other diseases could be made less common are even more obviously social matters and they are intrinsically desirable irrespective of their effect on the vital statistics Propaganda education and legislation by which it may be hoped that people will be immunized will avoid smoking and other bad habits and will seek medical advice as soon as certain symptoms develop must be inspired and organized by medical men but carried out by those specially appointed for the work Routine medical examination is the one prophylactic measure which requires the services of the individual doctor its good results are meagre indeed and ill-effects can easily follow from it in the prescription of futile treatment and in making people worried about defects of which they were happily ignorant before The idea of the general practitioner spending his time among healthy people and preventing them from becoming sick may be attractive but it bears no relation to the realities of this world Traditionally the doctor s function is to treat those with symptoms The uncritical acceptance of tradition has been responsible for much bad medicine but in this particular matter the traditional view is right

HEALTHY LIVING AND "POSITIVE HEALTH"

The view that we should do more than merely prevent actual diseases is now popular A vast proportion of mankind are it is said free of any identifiable disease process but they nevertheless feel chronically unwell They complain of being run down always tired generally off-colour or weak and are liable to vague indigestion aches and pains and headache It is hypothesized that such people often feel as they do because of their unhealthy habits of living and we are therefore urged to show them how to live healthily and thereby to achieve the state of positive health which is superior to the mere absence of ill health

To a large extent men s way of life is forced on them As medical men we can do nothing about the matter improvement can come only by social means But even in so far as men have the power to live in a supposedly healthy manner they often do not do so There may be nothing to stop them from going to bed early exercising regularly having a daily cold bath eating much raw fruit vegetables and wholemeal bread in an unhurried fashion avoiding tobacco and alcohol having a bowel motion at the same time each day and of having plenty of fresh air and sunshine Yet they do none of these things

Whether some of these features are in any way beneficial may well be doubted The belief that so called natural foods are superior to the refined and artificially coloured and processed foods which are widely eaten to day is based on a great deal of emotion and pseudo scientific quackery and a minimum of evidence The value of cold baths or of having a regular bowel motion at the same time each day is also questionable

On the other hand many people quite apart from any preconceived notions derive an immediate sense of well being from exercise fresh air and sunshine Some of this benefit is no doubt due to the bodily effects of these influences but much of it is due to the psychological effects The sight of the countryside bathed in sunshine is much more invigorating than the sight of the same countryside under a heavy pall of cloud Sunshine makes people s exposed parts brown and therefore makes them look fit and well" and more attractive to the opposite sex People feel much better after a walk in congenial company in beautiful surroundings than after a solitary walk through dismal city streets But some people rarely take exercise and if they do they claim that they feel no better for it

Those who complain of being always tired run down and generally unwell are as a rule depressed frustrated or worried those who feel full of energy and who are bright eyed and walk with head erect are the elated and the carefree But to identify health with happiness by saying that the former are living unhealthily and that the latter are positively healthy is to stretch the definition of health beyond all understanding Happiness rather than health is indeed the state for which men yearn And although severe and prolonged illnesses and particularly progressively fatal diseases prevent most people from gaining much satisfaction from life many benign

and even seems to show a preference for the well fed and vigorous It has also been suggested that state of mind may be as important as state of body in determining variations of individual natural resistance but this again is speculative

The problem of *acquired resistance* is equally tantalizing Some organisms as the result of an unsuccessful assault on the body confer on it a permanent, or solid resistance Second attacks of small pox for example are rare On the other hand immunity which follows a common cold is transient lasting only a few weeks This resistance which follows a spontaneous infection is called *naturally acquired active immunity* and it may be just as great after a symptomless latent infection as after an overt attack of the clinical disease Immunity due to latent infection accounts for the fact that many people never in their lives suffer an obvious attack of some of the common infectious diseases such as measles mumps or scarlet fever Nevertheless the fact that they have unknowingly been attacked can often be demonstrated by the finding of specific antibodies in the blood

Active immunity can also be acquired artificially The organism (or its antigenic moiety) is in a suitably modified form deliberately introduced into the body The modification prevents the development of clinical disease but does not interfere with the antigenic properties of the material so that it is able to stimulate the tissues to produce antibodies in sufficient quantities to ensure lasting immunity (*see* p 67) A less durable resistance can be achieved by administering the antibodies themselves this is known as artificial *passive immunity* (*see* p 67)

Closely bound up with the problem of resistance or immunity is that of *hypersensitivity* or *allergy* This also is an antigen antibody mechanism but one which produces a different result The entry of certain organisms into the body brings about after a short interval a state of tissue hypersensitivity to the particular organism When later a second contact with the organism occurs the response of such hypersensitive tissues is quite different from that of virgin tissues There is now as a rule intense inflammation out of all proportion to the dose of the infecting organism and particularly marked at the site of entry Many of the symptoms and signs that we associate with certain infections are in fact not due to the direct influence of the organisms themselves but are the result of this state of hypersensitivity For example the clinical manifestations of acute rheumatism are the product of a hypersensitivity reaction to the haemolytic streptococcus and are not caused by actual tissue invasion by the streptococcus No organisms can in fact be demonstrated in acute rheumatic lesions Hypersensitivity occurs in relation not only to bacteria and viruses but also to plants protein substances and drugs which can act as antigens in the same way But whereas hypersensitivity to organismal antigens is common hypersensitivity to vegetable or chemical antigens is unusual and confined to innately allergic individuals The reasons why some people are so unfortunate is obscure as is indeed most of this complex and baffling subject

Use is made of this phenomenon of hypersensitivity in detecting people who have been in contact with specific organisms (*see* p 72) The Mantoux test for example tells us whether or not an individual has been in contact with the tubercle bacillus (*see* p 346)

EPIDEMIOLOGY

This is the study of infectious organisms and infectious diseases as they affect populations in other words general trends rather than individual effects

There are two main factors which determine the prevalence of an infectious disease in a community There is the nature of the causal organism its virulence infectivity and catholicity Balancing this is the degree of natural or acquired immunity among the individual members of the community If a virulent organism is abroad and the general level of immunity low a widespread *epidemic* will probably occur If however immunity is high there will be only a few scattered *sporadic* illnesses Some epidemics arise as the result of the introduction from outside of an organism to which the community is unaccustomed but the majority are caused by the permanently present or *endemic* organisms and happen because of some disturbance of the general immunity virulence balance Knowledge of the factors which disturb this balance is very incomplete Little is known for example about spontaneous variation in the virulence of organisms But the remarkable decline in mortality and morbidity of most infectious diseases in Britain during the past fifty years is thought by many to be at least partly due to a general falling off in bacterial virulence Herd immunity is similarly subject to spontaneous variation for reasons that are only partly comprehended Environmental conditions certainly play a part Many epidemics are influenced by the weather and by the season of year Diseases such as measles and influenza which are largely spread by the inhalation of air borne droplets tend to be epidemic in the winter Those like

CHAPTER 7

Infectious Diseases

JOHN FORBES

INTRODUCTION

ALL diseases produced in man by the action of living organisms are infectious in the sense that they are potentially transmissible from one individual to another However in practice the term infectious disease is used to embrace only the more contagious disorders Others are sometimes called infective but this term has little significance

The relationship of Man to the very numerous organisms which exist on his every side is highly complex and far from being fully understood All kinds of permutation are possible There are *commensal* organisms which normally live a harmless parasitic life in the human body and yet which may at times turn and rend it There are others which exist in mutually profitable *symbiotic* partnership synthesizing valuable vitamins in exchange for their board and lodging There are extraneous and so called *pathogenic* organisms which when they enter the body may produce illness but they do not always do so nor do they invariably produce the same pattern of illness In dealing with infections it is possible to make some broad generalizations but it is rarely possible to predict with certainty what will happen when a particular organism comes into contact with a particular individual

The term infection by which is meant the entry of extraneous organisms into the human body is by no means synonymous with disease In fact the majority of infections are not associated with any overt symptoms It is only occasionally when particularly noxious organisms enter an unusually defenceless body that recognizable disease results In most infections the organisms are quietly destroyed by the bodily defences without a ripple on the surface Sometimes a brief battle is apparent there is some slight fever and malaise and the conflict ends without any familiar pattern of disease having emerged Such infections are often termed *abortive* Sometimes there is major war producing the classical infectious disease syndrome and ending in the death of one or other of the antagonists Sometimes the result is inconclusive Man emerges the apparent victor but all the organisms are not destroyed They linger on in relatively small numbers as parasites doing no harm to their host but potentially dangerous to his neighbours People who thus harbour pathogenic organisms are called *carriers* They may become carriers as the result of an infection which is either overt or symptomless and they may remain so either permanently or only temporarily

What determines whether or not an infection shall become a disease? There are two variables the invading organism and the invaded human host Organisms vary in *pathogenicity* that is in their ability to produce serious illness The organism of small pox for example often causes severe illness that of chicken pox rarely does They also vary in *invasiveness* which means the ability to spread widely throughout the body tissues As a rule the more widely invasive the organism the more severe the illness Organisms also vary in *virulence* Some virulent strains of diphtheria bacilli will produce grave disease while other less virulent strains may be almost harmless Linked with the property of virulence is the closely allied attribute of *infectivity* Some organisms or strains of individual organisms seem to be able to spread particularly easily from one host to another Highly infective organisms are usually but not always highly virulent also Finally the *number of organisms* that enter the body may be large or small The larger the number the greater the probability of consequent disease

On the other hand the human host varies in his reception of the organism We may as well admit at once that the mechanisms which would explain individual differences in *resistance* or *immunity* to infection are little understood *Natural* or *inborn resistance* may to some extent be racial but is more often an individual characteristic It varies considerably and often mysteriously in the same individual at different times It is often said that a poor state of general health will lower resistance and render a man more susceptible to disease but there is no proof that this is so In fact the virus of poliomyelitis often strikes down those in bounding health

brane abrasions or may enter through open wounds Some like the leptospira can penetrate the intact skin Such skin invasion is spoken of as infection by *inoculation*

Insect or animal vectors are often important agents in diseases acquired by inoculation The insect or animal may itself be infected by the organism or may simply carry it on its surface In either case the creature s bite provides the organism with a ready means of entry Insect vectors are also a factor in diseases acquired by ingestion for they sometimes carry infection from faeces to uncovered food In Britain to-day insect or animal borne dis eases are not common but many tropical fevers are spread in this way

Fomites are inanimate objects such as clothes bed linen books and toys which may become con taminated by infected discharges and thus be disease vectors The importance of fomites has been some what exaggerated and the perils of such things as cracked crockery in restaurants and books from public libraries have been over emphasized Con taminated sick room blankets sheets and handker chiefs are however potent sources of danger and the clothes of attendants can carry infection

Although some infections spread wholly or mainly by one particular method others habitually spread by a variety of methods For example in fluenza is transmitted as far as we know only by means of air borne droplets and enteric fever only by faecal or urinary contamination of food or fomites Poliomyelitis on the other hand probably spreads with equal facility by droplet infection and by faecal contamination

Control of Infection

Detection and Sterilization of Reservoirs

To prevent infectious disease from spreading within the community the logical first step is to locate and to sterilize reservoirs of infection Un fortunately this is a difficult task Overt cases of infectious illness are easy to detect and deal with but the symptomless carrier and the abortive dis ease present well nigh insoluble difficulties

Patients with manifest disease are usually *isolated* though the present day practice of isolation in Britain is not always entirely logical Scarlet fever once a killer but now a mild transient infection still must by law be isolated yet the equally in fectious streptococcal sore throat is legally free to roam at large However most infectious diseases produce such a degree of illness that the sufferer has to go to bed thus automatically isolating him self from all but his attendants and visitors If he is so ill as to require admission to hospital he will there be nursed in an isolation ward either alone or in company with others suffering from the same disorder At one time it was the custom to treat infectious diseases in special isolation or fever hos pitals but this practice has a number of disadvan tages and nowadays it is more usual to nurse the patients in an isolation block at a general hospital Ideally each patient should have a separate enclosed cubicle However even in the best regulated isola tion blocks there is always some risk of *cross infection* between patients with different diseases Thus it is usually better to isolate a patient in his home if conditions are suitable and he does not need special treatment available only in hospital

Isolation unfortunately cannot entirely prevent the spread of disease by patients with overt illness Often it can be applied only after the patient has already disseminated infection for many diseases are highly infectious towards the end of the incuba tion period that is before symptoms have appeared Moreover many people try to struggle on for a time even after the illness has begun before calling in the doctor This from a public health point of view is unfortunate because in many cases th degree of infectivity is greatest at the start and falls off fairly quickly during the course of the illness

How long patients should be isolated is debatable The period will of course dep nd on the nature of the infection In a few dise es like enteric fever and dysentery it is at least theoretically possible to determine by stool cultures when the patient ceases to be a carrier of infection But in most in stances such a determination is not possible In all probability however most infectious disease patients are a serious danger to others only during the acute phase of their illness In the past, patients have often been isolated for unnecessarily long periods Nowadays the tendency is to shorten the time and to release most patients from isolation as soon as they are convalescent

At one time a policy of *quarantine* used to be adopted for people who had been in contact with an individual who developed an infectious disease They were virtually isolated until it became clear that they had not acquired the disease Obviously this policy involved a good deal of hardship and it has now been largely dropped except when dealing with some of the more serious diseases such as smallpox and poliomyelitis Instead contacts are kept under close medical observation and isolated if and when symptoms appear Nor is it now cus

enteric fever which are spread by infected food and drink are at their height in the summer Mass movements of population and considerable alterations in the general state of hygiene and nutrition such as are likely to arise in time of war profoundly change herd immunity

The study of epidemic trends is made difficult by the fact that in most outbreaks only a few of those infected display diagnosable symptoms If every case of infection were detectable instead of only cases of obvious illness the task of the epidemiologist would be much easier As it is the apparently healthy carrier is usually difficult or impossible to detect yet his influence in the genesis of epidemics is almost certainly great There is good evidence that many epidemics are preceded by a rise in the carrier rate among the population a phenomenon which has sometimes been called a carrier epidemic

Epidemics frequently recur in fairly regular cycles though the periodicity may vary in different parts of the world In Britain for example measles epidemics have in the past tended to appear every other year The cause of this periodicity is unknown

Reservoirs of Infectious Organisms

If an infectious disease is permanently present or endemic in a community it is obvious that its causal organism must be finding permanent lodgement somewhere in the community When the disease is in an epidemic phase this lodgement is manifestly in the numerous infected individuals But when the disease is not epidemic and is occurring only sporadically most of the organisms are living quietly in or on a variable number of unwitting carriers Carriers are usually but not always human beings Some animals can be infected by and become reservoirs of organisms potentially harmful to man and like men they may become ill as a result or be unaffected in health Dogs for example may harbour the organisms of rabies and of leptospirosis canicola Cattle may be infected by brucellosis bovine tuberculosis anthrax and sleeping sickness Rats carry bubonic plague leptospirosis scrub typhus and rat bite fever Birds are the reservoirs of psittacosis and ornithosis There are others too which are mentioned later in the descriptions of individual infections Parasitic worms usually have a life cycle involving two hosts one of which is often man and the other an animal

Some organisms can survive for a time in soil and dust though desiccation and sunlight rapidly kill the majority However sporing organisms like *Cl tetani* can survive for years in suitable soil and the tubercle bacillus may remain viable for long periods in the dark and dusty corners of rooms Food may be infected but from its nature is usually only a temporary reservoir Stagnant water may harbour organisms However by far the largest reservoir of endemic infection is man himself

Methods of Spread of Organisms from Reservoirs

Organisms leave a human or animal reservoir in the various bodily discharges The exhaled breath and the faeces are predominant in this respect but *sputum nasal secretions urine seminal fluid* and breast milk can sometimes contain organisms A few infections such as venereal diseases are spread by direct bodily contact

Exhaled organisms are responsible for spreading most infectious diseases During coughing sneezing laughing and even talking fine droplets of mucus containing micro organisms are expelled from the respiratory tract These droplets can remain suspended in the air for a considerable time especially when the room is poorly ventilated and gentle air currents may waft them quite a long way Hence the risk to health of stuffy overcrowded buses and cinemas during the winter months when air borne infectious diseases are at their height Out of doors the risk is less for the wind disperses the droplets Apart from contaminating the air droplets also settle into the dust on the floor and furniture and infect it

Organisms discharged in the *faeces* readily contaminate the hands of a carrier at the time of defaecation and his hands may then convey them to food Modern sanitation and hygiene have made this method of spread less common but outbreaks of dysentery due to a carrier whose occupation involves the handling of food are still not infrequent Contamination of public water supplies by infected urine or faeces is now rare in Britain but sluggish rural streams in some parts of the country may be far from innocuous and bathing in them can be risky

Infected *spittle* on the ground will infect the dust which then is blown about by the wind to spread infection *Nasal secretions* may do the same but spread of infection from this source is more likely to occur through the soiling of hands and subsequent contamination of food *Seminal fluid* can sometimes be the vehicle by which venereal disease is transmitted and *breast milk* has on rare occasions been the means of carrying tuberculosis from a mother to her child

The organisms thus carried by bodily discharges enter the body of their next victim in various ways *Inhalation* of infected dust or of air borne droplets or *ingestion* of infected food are the commonest ways of acquiring infection However organisms may penetrate through minute skin or mucous mem

disease frequent washing helps to minimize the risk of acquiring disease by inoculation

Public health measures to reduce the incidence of those diseases that are acquired by ingestion include the purification of water supplies supervision of milk and meat production to ensure proper standards of hygiene inspection of food shops dairies and restaurant kitchens and proper treatment and disposal of sewage For details of such matters text books of public health and hygiene should be consulted

The spread of disease by infected sputum should not occur to any serious extent in civilized communities which usually discourage indiscriminate spitting Tuberculous patients are taught always to expectorate into a special bottle containing antiseptic Infected nasal discharges are more dangerous for the nasal carrier is usually unaware of his condition However routine use of handkerchiefs and frequent hand washing will minimize the risk

House flies are the most important insect vectors in Britain and should be destroyed by insecticides such as D D T and Gammexane Infected discharges should never be left in uncovered utensils for any length of time and food should always be kept in fly proof larders or refrigerators Rats and mice can sometimes carry infection and when found in buildings should be destroyed

Artificial Methods of Raising Resistance

Active and Passive Immunization So far we have been concerned with the control of infectious disease by attacking reservoirs of infection and by interposing barriers in the paths of spread between these reservoirs and potential victims A third method of prevention is possible and that is to raise the resistance of the potential victims by artificial means If this can be done the invading organisms will either find no lodgement or if they do will speedily be neutralized by antibodies

Artificial immunization is the process whereby susceptible people are protected by having the antibodies in their tissues artificially increased Active immunization stimulates the individual to increase his own existing antibodies or to develop new ones In passive immunization he is given antibodies which have been manufactured by other people or by animals Generally speaking active immunization is to be preferred for the raised resistance which results will last for a considerable time often years whereas the raised resistance after passive immunization is of short duration and usually lasts only a few weeks On the other hand active immunity takes weeks or even months to develop fully but passive immunity can be obtained almost at once

Bacteria and other organisms all contain *antigens* which are substances of a protein or complex carbohydrate nature and which when introduced into the human body cause it to produce antibodies Active immunization depends on the fact that it is possible by suitable means to modify the organisms in such a way that their virulence and pathogenicity are considerably reduced yet their antigenic properties are retained more or less intact Antigens are specific each one produces only one particular antibody It is therefore not possible to immunize an individual against a number of infections by giving him a single antigen Immunization by diphtheria antigen will stimulate the production of antibody against diphtheria only and none against smallpox or enteric fever Complete protection of an individual against a wide variety of infections by all available methods of active immunization is therefore a tedious business especially as some antigens must be given singly because they interfere with other antigens when mixed with them Fortunately this does not apply to all diphtheria whooping cough and tetanus antigens for example can be combined in a single injection The range of antigens suitable for administration is of course circumscribed and only a limited number of infectious diseases are as yet preventable by artificial active immunization The common cold influenza infective hepatitis mumps and many other diseases still baffle the immunologist but research on the problem is unceasing

The techniques of active immunization have been determined empirically and vary according to the disease Sometimes a *vaccine* of killed organisms is employed for example in the prevention of enteric fever and whooping cough The organisms are killed by heat by chemicals or by ultra violet light but their antigenic properties remain In some instances the vaccine is prepared from living but weakened strains of the organism Smallpox rabies yellow fever and tuberculosis vaccines are of this type Living vaccines produce excellent immunity but are understandably rather more risky than dead ones Occasionally modified bacterial toxin is used instead of the actual organism itself Such *toxoid* which is usually formalin treated toxin is employed in the prophylaxis of diphtheria and of tetanus

For passive immunization it is necessary to have a supply of *immune serum* that is blood serum which contains a high level of antibodies against the disease to be prevented Sometimes this can be obtained by actively immunizing an animal (usually the horse) Antisera for the treatment of diphtheria and tetanus are obtained in this way Sometimes the

tomary to close schools because of an outbreak of say measles or mumps but simply to watch all the children closely for the first signs of illness

Compulsory notification of infectious diseases is dealt with on p 69

Generally speaking the detection of symptomless carriers of infectious disease among the population at large is not yet a practical proposition The available tests would have to be a good deal simpler and more efficient than they are before the systematic examination of large numbers of apparently normal people could be expected to yield results commensurate with the expenditure of time and money that would be involved Carrier detection is however possible when the evidence suggests that the reservoir is one of a fairly small group For example localized outbreaks of infection in a relatively closed community like a hospital may suggest that there is a carrier among the staff or an outbreak among the customers of a particular dairy or food shop may be traceable to one of the employees

The problem of the carrier does not end with his or her detection for the sterilization of an established carrier may not be easy Antibiotics and chemotherapeutic drugs have enabled us to advance in this respect but even they are not very efficient Details of measures to be adopted for carrier sterilization are discussed under individual disease headings The human carrier still remains the chief headache of the epidemiologist and of the medical man charged with the task of preventing infectious disease

Animal and insect reservoirs are easier to deal with for sterilization is simply a matter of destruction As already mentioned the problem is a minor one in Britain but in tropical countries much time and money has to be spent on the elimination of mosquitoes tse tse flies and other insect vectors

Prevention of Spread from Reservoirs

As infectious organisms leave the body in the various discharges prevention of spread is a matter of preventing these discharges from reaching other susceptible people This in turn is a question of simple hygiene

The discharge of infected droplets from the respiratory tract can be much reduced if the patient sneezes and coughs into a large handkerchief or better still, into a disposable paper tissue The customary polite hand before the mouth when coughing is useless Properly made sterile surgical gauze masks will diminish droplet emission almost to zero but are uncomfortable to wear and are hardly practical for ill people However they should certainly be worn by attendants and visitors both to protect themselves and to protect the patient from possible cross infection Masks should be changed frequently for they lose their efficiency when moist and soon become contaminated by infected dust For this reason the wearing of masks by the general public during influenza epidemics is not likely to be very effective

Droplet and dust contamination of attendants clothes can be prevented if surgical gowns or overalls are worn These are put on when the nurse enters the sick room and doffed when she leaves Again it is important to discard the overall before it becomes heavily dust infected The wearing of dirty masks and gowns is worse than useless for it gives an entirely false sense of security In this connexion let it be said that the custom of so called barrier nursing of infectious patients in the general wards of hospitals has nothing but expediency to commend it Whenever infectious disease is diagnosed in a hospital patient the correct course is to isolate him without delay in a separate ward or cubicle

The spread of disease by infected dust can be minimized by strict cleanliness The oiling of blankets and floors with crude or medicinal paraffin effectively reduces the amount of fluff and dust in the air of wards and sick rooms but to be of any use it must be repeated at frequent intervals It is therefore not a very popular procedure

When the patient is better his sick room must be thoroughly scrubbed with soap and water and fresh air and sunlight must be let in to destroy any remaining organisms Such sterilizing procedures are sufficient for practical purposes and fumigation of the room with formalin vapour or with more modern antiseptic aerosols is seldom necessary Indeed after the minor infectious illnesses like rubella and chicken pox airing the room will alone be sufficient Infected bedclothes personal linen and overalls must always be sterilized by boiling or by steam under pressure in an autoclave before being laundered Fomites should be carefully washed and dried in the sun

When dealing with diseases which are mainly spread by organisms discharged in the faeces or urine and which are acquired by ingestion it is important to disinfect the dejecta before they are emptied into the sink or lavatory This is done by adding one of the antiseptic phenol derivatives such as Lysol (2 per cent) or Dettol Hand washing after defaecation is a habit which should be taught to all children and required of all adults Routine washing before meals is also a wise precaution Such personal hygiene is doubly necessary for people whose occupation involves the handling or preparing of food Apart from preventing faecal transmission of

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Public health measures to reduce the incidence of those diseases that are acquired by ingestion include the purification of water supplies supervision of milk and meat production to ensure proper standards of hygiene inspection of food shops dairies and restaurant kitchens and proper treatment and disposal of sewage For details of such matters text books of public health and hygiene should be consulted

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source is human blood being withdrawn from a patient who has recently recovered from an attack of the disease in question In the past *pooled adult serum* was sometimes used for passive immunization This was the pooled blood serum from a large number of people many of whom could be assumed to have had the disease and therefore to have antibodies against it in their serum But pooled serum had the drawback that occasionally one of the donors would unwittingly have in his blood the virus of homologous serum jaundice (*see* p 213) and then the disease would appear in the serum recipients Nowadays therefore instead of the whole serum we use the gamma globulin fraction only Gamma globulin which comprises 11 per cent of the total serum proteins contains most of the serum antibodies It protects almost as well as whole serum and carries no risk of serum jaundice Unfortunately a large amount of whole serum yields only a small quantity of gamma globulin which is consequently scarce and expensive

Passive immunization can be carried out when immediate immunity is urgently needed for example to protect weakly infants or pregnant women who have come into contact with overt cases of infectious disease In such circumstances active immunization would not help for resistance would develop too slowly to prevent illness Often in these cases active and passive immunization are performed simultaneously The passive immunity obtained protects against the immediate danger and the active immunity protects against similar future contacts

Antitoxic immune serum is given to patients with diphtheria and to those with wounds which may have been infected with tetanus organisms It should be noted that although we speak rather loosely of diphtheria and tetanus antitoxins as being used in the treatment of these diseases in point of fact the antitoxins can do nothing to combat any toxins which have already been formed What they do is to passively immunize the patient against *any further toxins* that are produced by the invading organisms It is therefore vital to give antitoxin as early as possible in these diseases once large amounts of toxin have been formed and have been fixed to the tissue cells antitoxin has little value

Active immunization is a procedure relatively free from risk except in the rare instance when some error arises in the preparation of the antigen The giving of gamma globulin is equally safe but passive immunization with serum from non human sources always carries some risk of a hypersensitivity reaction (*see* p 63) to the foreign animal serum proteins Rarely but especially in allergic individuals who suffer from asthma hay fever and the like an immediate *anaphylactoid reaction* occurs after the serum injections There is collapse pallor vomiting a marked fall in blood pressure and the patient may become unconscious Death however is very unusual This alarming reaction is more likely to happen if the serum is given intravenously instead of subcutaneously or intramuscularly and especially if one omits first to warm the serum to body temperature Treatment consists of anti shock measures warmth artificial respiration oxygen and subcutaneous adrenaline (0 25 to 1 ml of a 1 1 000 solution) or better still intravenous noradrenaline (4 mg in each litre of a normal saline infusion) It is wise before giving antiserum to a known allergic individual to inject 0 1 ml of the serum intradermally Any local reaction in the shape of an erythema or urticarial wheal contraindicates further serum injection

More common than an immediate anaphylactoid reaction is delayed *serum sickness* This is seldom serious and never fatal About ten days after the serum injection mild pyrexia develops accompanied by an urticarial rash which starts at the site of injection but later becomes general There may be vomiting joint pains and lymph gland enlargement Polyneuritis and flaccid paresis of the injected limb are uncommon complications The sickness usually resolves spontaneously in a few days though neurological complications may last for weeks or even months Treatment is therefore hardly necessary but if the urticaria is severe it can be relieved by anti histamine drugs such as promethazine hydrochloride (Phenergan) 25 mg twice daily by mouth

It might be supposed that untoward serum reactions would occur only in patients who had been sensitized by previous injections of animal sera It is true that most serum injected patients do after a latent interval of 10 days or so develop a hypersensitive state though this hypersensitivity wanes again during the next 2 or 3 years Further serum if given during this hypersensitive phase is likely to cause a reaction But in practice it is found that reactions are just as common among patients who have never previously had serum injections and one can only assume that they have become sensitized in some other way

Nowadays serum reactions are rare in Britain because diphtheria and tetanus the only two diseases for which animal derived antisera are widely used are uncommon The former has been largely abolished by active immunization in childhood and the latter has always been a rare disease

Chemoprophylaxis The prevention of infectious disease by large scale prophylactic dosing of susceptibles with sulphonamides or antibiotics is a tempting idea but it is not to be recommended

Such experiments as have been carried out along these lines have proved disappointing in that their success seems to be only temporary and a serious objection is that such a policy encourages the survival and multiplication of drug resistant organisms By common consent therefore chemoprophylaxis is reserved for individuals for whom infection carries a special risk For example children with rheumatic heart disease are often given continuous prophylaxis to reduce the risk of their acquiring fresh streptococcal infection which might reactivate their rheumatism Pre operative antibiotics which are used particularly when intestinal surgery is contemplated will lower the risk of subsequent invasion by intestinal organisms Used in this sparing way chemoprophylaxis is unlikely to create widespread resistant strains of virulent organisms

General Hygiene

Individual resistance to infectious disease is unquestionably higher in communities that have a high standard of public and private hygiene Such high hygienic standards go of course with a high standard of living generally and it is impossible to say how much credit for the immunity should go to better hygiene and how much to better food better housing conditions better clothing and so forth But that social conditions are a major factor *in the incidence of infectious disease is clearly* shown by statistics of mortality from such diseases in different classes of the population those for the lower social scales are very much higher

It would be unjustifiably complacent to attribute the general decline of infectious disease in Britain during the past hundred years entirely to improved standards of living Changes in the virulence of organisms alterations in social habits the growth of artificial immunization better diagnosis and treatment have all played a part Nevertheless the epidemics of cholera typhus and bubonic plague that once used to rage in Britain have now disappeared and there can be little doubt that this has largely been due to better housing sanitation and cleanliness

Major wars in the past by causing disruption of social services and a general lowering of living standards have usually been followed by a devastating pandemic of infectious disease Typhus used to be *the common scourge but after World War I in*fluenza took its place No serious epidemic of infectious disease followed World War II however partly because threatened outbreaks were nipped in the bud by vigorous public health measures In more than one way World War II may prove to have been a turning point in civilization

Education of the public in personal hygiene is of great importance *Children should be taught to use* handkerchiefs to wash their hands after defaecation and before meals to avoid communal towels whenever possible and to maintain high standards of personal cleanliness and domiciliary hygiene Progress is slow and is handicapped in this country by the common delusion that Britons are a naturally clean race and in this respect compare favourably with all foreigners That this is a myth can be seen by comparing food shops and public lavatories in Britain with those of North American (and of many European) countries Nevertheless progress there is

Compulsory Notification of Infectious Diseases

Since 1889 certain infectious diseases have in Britain been by law notifiable to the local Medical Officer of Health Responsibility for such notification rests with the head of the household in which the disease occurs and with the attending medical practitioner in practice the latter usually carries out this duty and is paid a statutory fee for doing so The list of notifiable diseases is an arbitrary one but it includes most of the common fevers Local authorities have power to add to the list if circumstances in a particular area seem to demand it

The following diseases are always notifiable—

Cholera	Pemphigus neonatorum
Diphtheria	Plague
Dysentery amoebic and bacillary	Pneumonia acute primary and acute in*fluenzal*
Encephalitis lethargica	Poliomyelitis
Enteric fevers	Puerperal pyrexia
Food poisoning	Relapsing fever
Malaria	Scarlet fever
Measles	Smallpox
Meningococcal infections	Tuberculosis
Ophthalmia neonatorum	Typhus
	Whooping cough

It is doubtful if compulsory notification does anything to check the spread of infectious disease The original idea was that prompt notification would lead to early isolation of cases and thus help to *prevent epidemics But* unidentified carriers and abortive or misdiagnosed cases nullify this aim to a large extent However notification is useful to the epidemiologist in that it helps him to follow the general trend of infectious disease in the community

GENERAL CLINICAL MANIFESTATIONS OF INFECTIOUS DISEASE

The actual entry of pathogenic organisms into the body does not as a rule produce any symptoms For a time nothing seems to be happening but the organisms are nevertheless quietly multiplying until eventually the symptoms and signs of disease appear The interval between the initial invasion and the start of symptoms is termed the *incubation period* Its length varies with different diseases and may be less than a week as in the case of scarlet fever or as long as 3 weeks as in mumps or chicken pox In some diseases it is fairly constant but in many it varies within wide limits

The first symptoms of an infectious fever are often non specific and are termed *prodromal* (Gr prodromos=running before) in the sense that they precede the characteristic symptoms and signs of the disease Such symptoms include headache general malaise shivering or chilliness loss of appetite nausea or vomiting and aching in the back and limbs Infants sometimes have a fit The body temperature is raised but is not usually as high as it becomes later

After a day or two specific symptoms and signs usually appear unless the infection is an abortive one Sometimes these symptoms and signs are at the original site of invasion in diphtheria for example the throat is sore and in erysipelas there is spreading inflammation round the point of inoculation Sometimes the manifestations are in a quite different situation Meningococcal infection for instance is acquired by droplet infection via the upper respiratory tract yet the respiratory symptoms are trivial and the disease shows itself chiefly in the central nervous system Sometimes as in brucellosis the signs and symptoms remain generalized throughout the illness

In many infectious fevers a characteristic and diagnostic *skin rash* appears at a certain point in the illness

With the full development of the specific manifestations the pyrexia reaches its highest point and the disease is said to be at its *acme* Death may result but if not the illness then declines symptoms and signs gradually disappear the temperature becomes normal and the patient is *convalescent* In some diseases this decline may be interrupted by temporary *recrudescence* of symptoms and pyrexia in others *relapses* may occur even after the patient is apparently well again Such relapses are not usually as severe as the first onslaught

Nowadays the full or classical clinical picture of many infectious diseases is not often seen This is sometimes the result of artificial immunization which if waning or incomplete may permit a mild attack Moreover improved laboratory techniques have allowed earlier diagnosis and treatment and many illnesses can thus be nipped in the bud The prevalent but questionable habit of treating any pyrexial illness immediately with antibiotics also tends to modify the clinical picture of many infectious diseases often out of all recognition though most virus diseases being insusceptible to antibiotics can still be seen in their classical form Spontaneously abortive infections do not of course progress beyond the phase of prodromal symptoms

In former days *fulminating toxic* and *haemorrhagic* varieties of some infections were described Modern therapy has almost abolished these severe variants

Diagnosis The diagnosis of infectious diseases is in the main a clinical matter Laboratory investigations are often useful but they do take time are liable to error and their results may sometimes be difficult to interpret Bedside diagnosis should be possible in most infections

Early diagnosis is particularly desirable in infectious diseases because they tend to progress rapidly when specific treatment is available its prompt application will prevent severe illness Moreover early isolation is desirable for it is in the early stages of the illness that infectivity is at its height

Diagnosis is of course easier during an epidemic when even atypical or abortive cases may be correctly identified Sporadic infections are more difficult Sometimes however there is a history of contact with an infectious patient The incubation period of the disease being known symptoms which appear at the expected time will almost certainly be due to the same disorder In the absence of such a guide and when faced with a patient in the prodromal stage of an infection usually all one can do is to wait a day or two until the specific symptoms and signs appear Fortunately acute infectious diseases when unmodified by artificial immunization or by premature treatment do on the whole run true to type In contrast to a disorder like disseminated sclerosis which may present in a variety of ways measles or meningococcal meningitis produce much the same clinical picture in all patients

The Rash One group of infectious diseases the *exanthemata* almost invariably produce a characteristic rash It may not be confined to the skin but may also appear on mucous surfaces Sometimes the mucous membrane rash or *enanthem* precedes the skin rash or *exanthem* and its recognition will result in earlier diagnosis The buccal Koplik spots of measles for example are as typical of the disease as the later macular skin eruption

When examining a rash in a suspected case of infectious disease observe first of all the kind of lesions that are present They may be all of one sort (allomorphic) or of diverse kinds (pleo morphic) They may be erythematous macular petechial papular nodular vesicular bullous pus tular or urticarial An *erythema* is a uniform redness of the skin due to dilatation of the surface capillaries and it blanches on pressure When it consists of a number of small pin point spots it is called a *punctate erythema* A *macule* is a dis coloured area usually either red or brown not raised above the level of the surrounding skin A *petechia* is a pin point haemorrhage into the skin Large numbers of petechiae are often described as a *purpuric rash* Macules and petechiae do not blanch on pressure A *papule* is a raised macule feeling solid to the touch and either flat, rounded or pointed *Nodules* are simply large papules *Vesicles* are very small blisters containing clear serous fluid An ordinary blister is in medical jargon a *bulla* or *bleb* A *pustule* is a vesicle containing purulent fluid An *urticarial wheal* is a white elevation of the skin surrounded by an erythema it is part of the well known "triple response of the skin to the liberation of histamine like substances in it

The next thing is to study the distribution of the rash Not only should the general topography of the lesions be observed but the area in which they first appear and the way in which they spread to other areas The distribution may be important For example smallpox and chicken pox have super ficially similar lesions but in smallpox they are more profuse towards the extremities whereas in chicken pox they are thicker on the trunk Most infectious disease rashes spread centrifugally start ing on the head and neck spreading to the trunk and finally invading the limbs A rash which starts on the hands or feet is unlikely to be caused by an infectious fever

Infectious disease rashes rarely itch which is help ful in distinguishing them from allergic eruptions and from some kinds of skin disease

In the recognition of rashes and indeed of infec tious diseases as a whole an ounce of experience is worth a pound of book learning Rashes are usually so typical that when they have been seen once or twice they can thereafter be identified almost at a glance As a rule difficulty arises only with the rarer and less familiar disorders such as smallpox Never theless the mistake should never be made of con sidering a rash by itself without reference to the history and the rest of the clinical picture Skin eruptions which result from allergic reactions to chemicals or antibiotics may imitate the rashes of such fevers as measles and scarlet fever but the accompanying symptoms and signs will be quite different

Laboratory Investigations Although of secondary importance compared with clinical findings labora tory tests are often useful to confirm the diagnosis Occasionally when the clinical picture is not clear cut they may be crucial

One group of laboratory procedures is concerned with detection of the causal organism in the body fluids or discharges Throat swabs are examined in diphtheria and scarlet fever to identify *C diph theriae* or the haemolytic streptococcus Cough plates are used in whooping-cough to demonstrate *H pertussis* in the exhaled droplets Blood cultures are made in a variety of disorders Cerebro spinal fluid is examined to find the organism responsible for a meningitis Stool and urine cultures can reveal the presence of dysenteric or enteric organisms Specimens of serum from vesicular pustular or ulcerative skin lesions sometimes contain the in vader Organisms can often be found in pathological exudates such as a pleural effusion

When interpreting the results of such tests how ever two things must be remembered Failure to find the expected organism does not invalidate a firmly-established clinical diagnosis and the pres ence of organisms only indicates infection and not necessarily disease If for example clinical evidence strongly indicates the presence of tuberculous meningitis appropriate treatment should be given even if no tubercle bacilli can be found in the cerebro spinal fluid On the other hand the finding of typhoid organisms in a patient s stools does not necessarily mean that he is suffering from typhoid fever he may simply be a chronic typhoid carrier Only when organisms are found in the blood or cerebro spinal fluid can one be sure that their pres ence signifies infectious disease for in well people these fluids are always sterile

The second group of laboratory tests is immuno logical The tests are designed to show the presence of circulating antibodies from whose existence one can sometimes infer the additional presence of anti gens that is of infecting organisms or their toxins Here again interpretation of results needs caution Antibodies which have been produced by an overt or latent infection or by artificial active immuniza tion sometimes persist for many years Thus a demonstration of their presence may simply mean that infection has occurred at some time in the past and is no guarantee of present infection However if the test is repeated a few days later and if the level of antibodies is found to be higher obviously there is active antibody manufacture going on From this it can be fairly confidently assumed that an

antigenic stimulus is currently at work and that therefore there is active infection present

Tests of this kind are usually done on blood serum and include the *precipitation agglutination* and *complement fixation* reactions which take place when an antigen is added in the laboratory For technical details a textbook of bacteriology should be consulted The kind of test depends on which disease is suspected but agglutination tests are most frequently called for One negative antibody detection test does not invalidate a clinical diagnosis especially if it is done in the early stages of the illness Detectable antibodies are often slow to appear and repeated tests at intervals may be needed before they can be demonstrated

Circulating antibodies can also be detected by certain skin tests of which the best known and most often used is the Schick test (*see* p 76) Such skin tests are not quantitative so they are not of much assistance in the diagnosis of active disease Their value lies in the identification of susceptible individuals that is people who have no natural antibodies against the disease in question Such people are therefore candidates for artificial active immunization

Similar skin tests are used to detect allergic hypersensitivity to an organism The presence of hypersensitivity indicates that the individual has at some time or another been infected by the organism An example is the Mantoux test (*see* p 346) which is used in tuberculosis Skin sensitivity tests are also used to discover individual allergy to plant pollens foods inert materials and similar non bacterial allergens However skin tests as a whole are not of much value in the diagnosis of active infectious disease

The last group of laboratory tests assists diagnosis indirectly These tests aim at discovering in the blood or other tissue fluids evidence of anti bacterial defence mechanisms (other than antibody formation) or of changes which can be ascribed to the presence of organisms The tests are non specific and do not identify the particular organism with certainty Nevertheless from the pattern of changes a shrewd guess can often be made as to the probable invader

A white blood cell count for example is often helpful The large group of diseases resulting from coccal infection is characterized by a granulocytosis Bacillary and virus diseases on the other hand have little or no effect on the number of circulating granulocytes Whooping cough is accompanied by a lymphocytosis glandular fever by a monocytosis Eosinophilia is common with infestations by animal parasites Severe leucopenia can occur with an overwhelming infection and may thus be a bad prognostic sign However there are frequent exceptions to all these statements and a clinical diagnosis is never destroyed but only tested by an unexpected white blood cell count

The appearance and numbers of the red blood cells are not as a rule affected by infectious diseases but their sedimentation rate is increased The erythrocyte sedimentation rate (E S R or B S R) can be similarly augmented by a variety of physiological and pathological conditions so its value in the diagnosis of infection is largely negative in that a normal reading more or less excludes the presence of significant infectious disease In chronic infections such as tuberculosis it may help to assess the activity of the disease

Other laboratory tests on the blood are occasionally useful for example the serum proteins may be abnormal in severe infective hepatitis

Tests carried out on the cerebro spinal fluid include cell counts protein estimation and measurements of the glucose and chloride content Significant and diagnostic changes may be found in infections which involve the central nervous system

Occasionally the examination of pathological exudates may assist diagnosis For instance pleural effusions which are the result of coccal infections usually contain large numbers of granulocytes whereas those due to viruses or to tuberculosis tend to be lymphocytic

Treatment Apart from the question of isolation and other measures that are designed to limit the spread of infection the treatment of infectious diseases differs in no way from that of any febrile illness Specific treatment if available is used to destroy the invading organisms as quickly as possible Non specific treatment aims at making the patient comfortable at minimizing the degree of tissue damage and at conserving the patient s strength so that his convalescence will be short Specific methods of treatment will be described under the headings of individual diseases it is with non specific treatment that this section is concerned

Rest in bed is necessary for severe illnesses but children with mild attacks of minor infections such as rubella and chicken pox can usually remain up and about Patients in bed should be allowed to choose their own posture when able to do so and should not be compelled for theoretical reasons to lie flat when they feel more comfortable sitting up Very ill people who are unable to fend for themselves are usually happiest in a supine semi recumbent position but cases of meningitis often prefer to lie flat and on one side The routine practice of nursing febrile patients between blankets is to be deprecated It is necessary only when they

are sweating profusely at other times it causes discomfort.

Anyone who is really ill will require assistance with feeding and will have to be washed once a day Particular attention must be paid to pressure points (shoulders sacral area and heels) in order to avoid bed sores and helpless patients should be turned from one side to another at frequent intervals Fortunately specific treatment of most of the infectious diseases that occur in Britain is nowadays so effective that grave illness is uncommon the grim spectacle of advanced febrile toxaemia with its muttering delirium wasted limbs and helpless incontinence is very rarely seen

As most sufferers from infectious diseases are young peripheral phlebothrombosis is an uncommon complication Nevertheless patients in bed should always be encouraged to move their legs frequently in order to avoid venous stagnation If the period of bed rest is likely to be prolonged a rigid padded foot board should be used to prevent foot drop for this purpose pillows are useless For the same reason nurses should be discouraged from tucking the bedclothes tightly round the patient s feet On the other hand cradles to lift the clothes from the feet and legs though admirable in theory are unpopular with patients because they let their feet get cold

Recovery from most infectious diseases is rapid so the convalescent period need not be prolonged Progressive active exercises will hasten recovery but elaborate physiotherapy is required only after paralytic infections such as poliomyelitis Effort syndrome (*see* p 290) is not uncommon in neurasthenically inclined people after acute fevers but usually disappears with vigorous reassurance and encouragement

The traditional recommendation for a fever diet is that it should be light but nourishing In practice the patient s appetite is the best guide and there is no advantage to be gained from forcing an unwilling invalid to eat unwanted food Equally there is no point in restricting a comparatively healthy child with mild chicken pox to slops Most ill people will spontaneously reject unsuitable dishes and will tend on the whole to favour milk and egg preparations meat soups sweet custards and fruit but individual tastes vary Attractive presentation will do much to stimulate a jaded appetite and at least as much thought should be given to the preparation as to the substance of the diet Additional protein in the shape of various proprietary extracts is theoretically desirable because fever is accompanied by increased protein katabolism However it is doubtful whether extra protein feeding is necessary in practice except in acute poliomyelitis or in unusually prolonged and severe cases of enteritis when hypoproteinaemia may be a feature Fluids should not be forced into patients but a fluid intake somewhat in excess of the normal two or three pints daily is usually demanded if there is marked pyrexia and increased fluid loss by sweating Sweetened fruit juices are usually popular and glucose as the sweetening agent is often preferred to cane sugar because the resulting drink is not so sickly Glucose has contrary to popular belief no other dietary virtue Unless previous undernutrition has produced undoubted vitamin deficiency vitamins are of no value in the treatment of acute infectious illness

Patients who are ill febrile lacking in appetite and confined to bed are normally constipated and no attention need be paid to the fact unless and until the patient complains of abdominal discomfort Satisfactory evacuation can then nearly always be achieved by an enema of normal saline Chemical purgatives should be avoided unless the patient is accustomed to taking them regularly and even then they should not be given if he is seriously ill Mechanical laxatives such as liquid paraffin and petroleum emulsion are less objectionable but their use should never be a matter of routine Whenever possible patients should be allowed to use a bedside commode for defaecation A commode is more comfortable than a bed pan and if anything calls for rather less effort to use it

Little in the way of non specific drug treatment is required in most present day infectious diseases Aspirin 0 3–1 g (5–15 gr) or Codeine Compound tablets 1–3 can be used to relieve headache and limb pains An unfashionable but worthy veteran is Dover s powder (Pulv Ipecac et Opii B P) 0 3–0 6 g (5–10 gr) Barbiturates such as amylobarbitone 0 06–0 18 g (1–3 gr) or quinalbarbitone in the same dosage promote sleep and the former is also useful for the daytime sedation of anxious patients with poliomyelitis The drug treatment of special symptoms is described in the pages devoted to individual infectious diseases

P U O

Every practising physician is familiar with the child or adult who develops fever headache anorexia some vomiting perhaps and vague aches and pains who never displays any localizing symptoms or signs in whom all laboratory tests are negative and who gets better in a week or so without having vouchsafed a clue as to the nature of his complaint If there happens to be in the neighbourhood an epidemic of poliomyelitis or of glandular fever or perhaps of enteric fever he will probably be regarded as an abortive case of the epidemic illness and no doubt this conclusion will

often be correct If there is no such epidemic he will usually be labelled vaguely as flu gastritis or some such But honesty compels us to admit that the label should be P U O (Pyrexia of Uncertain Origin)

Many of these mysterious infections are indeed attacks of one or other of the common infectious diseases They are more likely to be of virus origin because coccal and bacillary infections are more easily identified by laboratory tests than are virus disorders Laboratory tests for virus antigens or antibodies are technically complicated and laborious If the pursuit be dogged enough a positive identification may eventually be forthcoming usually some weeks after the patient has recovered In many instances despite all efforts the result is negative Undoubtedly there are pathogenic viruses still unknown Some are perhaps anomalous strains of known organisms others may be undiscovered species It is quite probable that some cases of P U O are infections by such viruses

It goes without saying that every effort must be made to establish a diagnosis P U O is not a diagnosis but a confession of ignorance Not a few pyrexial illnesses can sometimes be very puzzling at the start though sooner or later the vigilant observer will be rewarded by an enlightening clue Tuberculosis enteric fevers brucellosis subacute bacterial endocarditis occult pyogenic abscess leptospirosis unfamiliar tropical diseases some malignant growths Hodgkin s disease and myelomatosis are a few examples of disorders which at first may present as P U O However diseases of this kind presenting in this way are relatively rare The brief mysterious P U O of the type described above is very common

Little can be done in the way of treatment except to isolate the patient treat the symptoms and reassure the anxious relatives that the condition is probably not serious Thanks to modern treatment death from infectious disease is rare in Britain to day except when the patient is already debilitated from some other illness At the present time poliomyelitis is the principal public bogey among infectious diseases and in a P U O is usually the condition suspected and feared by the patient and his family It is admittedly often difficult to be sure that a P U O will not turn out to be poliomyelitis and indeed some cases probably are in fact non paralytic poliomyelitis infections This diagnostic problem is more fully discussed on p 400 But except during poliomyelitis epidemics the chances that any given P U O will prove to be *paralytic* poliomyelitis are small

Antibiotics should not be given unless there are strong reasons for suspecting the presence of a known antibiotic sensitive organism or unless the patient is alarmingly ill The giving of antibiotics blindly in all undiagnosed ferbrile illnesses is a widespread but regrettable practice It obscures the clinical picture leads to the propagation of antibiotic resistant bacterial strains and is a great waste of money

INDIVIDUAL INFECTIOUS DISEASES

Septicaemia

Septicaemia means invasion of the blood stream by infecting organisms Pathologically speaking it is a very common condition for in most infectious illnesses there is a phase when careful culture will demonstrate the invader in the blood The majority of organisms spread from their point of entry to other parts of the body via the blood stream Recent research has shown that this happens even in infections like poliomyelitis which formerly were thought not to be associated with septicaemia (The term bacteraemia has sometimes been employed to describe a symptomless septicaemia but its use offers no great advantage)

In clinical practice we are accustomed to use the term septicaemia in a narrower sense By it is meant an illness in which a virulent organism is multiplying rapidly in the blood and which is accompanied by a number of fairly characteristic symptoms and signs In other words clinical septicaemia is simply a *severe* septicaemia due to the combination of a virulent organism and a patient with low resistance The more the scales are weighted against the patient the more acute and fulminating the septicaemia symptoms will be Thus an acute and rapidly fatal septicaemia is a not infrequent conclusion to a long and debilitating illness or used to be till antibiotics came into the picture

In theory almost any organism could given favourable circumstances produce clinical septicaemia In practice the condition is most frequently associated with the cocci probably because these organisms are so widespread in their distribution and are always at hand to seize any opportunity for mischief Nevertheless *Salmonella typhi Brucella melitensis E coli* and *Bacillus anthracis* may on occasion produce clinical septicaemia and there are others which infrequently do so On the other hand the toxin producing organisms like *Corynebacterium diphtheriae* and *Clostridium tetani* rarely if

ever invade the blood stream preferring to remain localized at the site of infection and to do their fell work by means of their circulating exotoxins

Clinical Picture Certain symptoms are common to all septicaemias whatever the causal organism A patient who is suffering from pneumonia perhaps or has an infected wound or who is in the throes of a chronic illness starts to complain of cold shivers marked headache and increasing weakness His temperature previously moderate begins to rise to high levels (103 –105 F) there it may be sustained or it may swing up and down The pulse rate quickens There may be nausea or vomiting sometimes diarrhoea Sweating is profuse with consequent dehydration and a dry tongue covered in brown fur The urine becomes scanty and albuminous

As the septicaemia worsens the patient s condition deteriorates He loses flesh rapidly his eyes are unnaturally bright and his sunken cheeks unhealthily flushed He becomes disorientated restless and delirious and a petechial rash may appear on the skin Shivering attacks or *rigors* are frequent The spleen is often palpable and there may be slight jaundice Heart murmurs sometimes develop Some varieties of acute septicaemia notably that due to the meningococcus may be associated with profound circulatory collapse the result of haemorrhage into the adrenals (Waterhouse Friedrichsen syndrome *see* p 128) Without treatment the patient almost always dies after a week or two

Sometimes when the organism is less virulent and the patient s resistance higher the symptoms are less severe the course of the illness is more prolonged and spontaneous recovery may take place On the other hand septicaemic infections in debilitated old people can slay the patient in two or three days

Diagnosis This is not as a rule difficult The obvious deterioration of the patient and the growing evidence of generalized dissemination of infection should lead to immediate blood culture and this will invariably disclose the organism It is important however to take the blood culture before antibiotic treatment is begun otherwise the result may be negative If the patient is already on antibiotic therapy when the signs of septicaemia develop the drug should be omitted for 48 hours before taking the culture It is obviously not being therapeutically effective anyway

Treatment Prompt treatment with an appropriate antibiotic will unless the organism is unusually resistant result in immediate improvement The antibiotic should be given in full doses and by the most efficient route penicillin for example should be given intramuscularly and not orally Antibiotic treatment has entirely changed the outlook for patients with severe septicaemia or blood poisoning as the general public calls it Nowadays a fatal outcome is rare unless the patient is very old or feeble Nevertheless it is not certain that this happy state of affairs will continue permanently Already a number of deaths have been reported from different parts of the world as the result of septicaemia due to antibiotic resistant strains of staphylococci One organism at least is fighting back

Fluid replacement is important in a severe hyperpyrexial illness of this nature If vomiting or delirium make it impossible to give an adequate amount by mouth normal saline with 5 per cent glucose should be dripped continuously into a vein Restlessness and apprehension are best allayed by morphine 10–16 mg (1/6th–$\frac{1}{4}$ gr) if necessary every 4 or 6 hr The addition of hyoscine hydrobromide 6 mg (1/100th gr) is advisable when there is delirium

Patients with severe septicaemia need constant skilled nursing and admission to hospital is usually necessary Surgery is occasionally required to deal with metastatic abscesses that may develop when the organism is a pus forming one Septicaemia *with multiple abscess formation is sometimes called pyaemia*

Bacterial Diseases

A Those Acquired by Inhalation

Diphtheria

The disease is endemic in Britain and in the past epidemic outbreaks were common Diphtheria is however an outstanding example of an infectious disorder which has been largely stamped out by preventive active immunization and to day this quondam killer is a rare and seldom severe disease

The causal organism is the *Corynebacterium diphtheriae* (Klebs Loffler bacillus) which usually attacks the throat but occasionally invades the nose vagina and other mucous surfaces Rarely it may contaminate open wounds The infection is spread by droplet spray from carriers with the organism in their throats nasal and aural carriers are less common The bacteria can persist for weeks on clothing toys or household utensils

There are three pathogenic strains of diphtheria bacilli gravis intermedius and mitis All produce an exotoxin but the gravis strain produces an endotoxin as well so that infections with this strain are

more severe Mitis strain infections are very mild There are in addition other strains which are almost avirulent and these strains are not infrequently found in healthy throats The mere finding of morphological diphtheria bacilli in the throat of a patient with tonsillitis therefore does not necessarily mean that he is suffering from clinical diphtheria

Diphtheria is most common in children under 10 Infants up to 6 months are usually immune thanks to maternal antitoxin derived *in utero* but the immunity gradually wears off as the child gets older Although most adults have acquired immunity by overt or subclinical infection in childhood diphtheria in adults is not unknown

Susceptibility to the disease can be demonstrated by the *Schick test* in which standardized diphtheria toxin is injected intradermally The dose is 1/50th of the minimum lethal dose for a guinea pig If the injected individual has in his blood more than 1/30th of a unit of antitoxin per ml the antitoxin will neutralize the injected toxin and no reaction will occur the Schick test is negative If on the other hand he has less than this amount of antitoxin redness and oedema will appear round the injection site after about 24 hr and will persist for 4 or 5 days This is a positive Schick reaction and indicates susceptibility to diphtheria

Sometimes when the subject is sensitive to bacterial products in the toxin though not to the toxin itself a false positive reaction may appear To avoid confusion therefore a control injection of heat inactivated toxin is given in another site at the same time as the injection of active toxin If the subject is truly susceptible his reaction to the active toxin will be greater than the reaction to the heat destroyed toxin

C diphtheriae remain localized at the site of invasion and never produce a septicaemia Their toxins however circulate in the blood stream and are responsible for the general effects of the disease

Clinical Picture The incubation period is usually 2 or 3 days

The illness begins with malaise moderate pyrexia (up to 100 F) and a slightly sore throat Despite the comparatively mild symptoms however the patient looks ill and toxic and his pulse rate is quick On examining the throat the characteristic diphtheritic membrane will usually be seen though on rare occasions when a very severe gravis infection is present the membrane may be absent The membrane is a dirty yellowish grey in colour has crenated edges and is firmly adherent to the underlying mucous surface and difficult to remove The severer the infection the greater is the area of membrane In mild cases it is confined to one tonsil In severe cases it may spread to both tonsils to the soft palate and to the pharyngeal wall Surrounding inflammation is negligible

There is usually some enlargement of the cervical lymph glands and in gravis infections this may be extreme Tenderness is not marked

Diphtheria which extends to the larynx is rare to day but in such an event the consequent membranous obstruction to breathing can be dangerous Stridor is the first sign of such obstruction Later signs of severe respiratory embarrassment appear cyanosis violent efforts at inspiration in which the accessory muscles of respiration are brought into play and sucking in of the suprasternal hollow and intercostal spaces Unless the obstruction is relieved death from asphyxia follows

Nasal diphtheria is rare and never serious The patient usually a child presents with a sore running nose On examination there is crusting of the anterior nares and a diphtheritic membrane is often to be seen inside the nostrils Diphtheria of other mucous surfaces or of wounds often produces a puzzling chronic infection without characteristic appearances and like nasal diphtheria is frequently only diagnosed after swab culture

Course and Complications Many mild cases of diphtheria would probably if left to themselves recover spontaneously after 10 or 14 days However as the disease is potentially lethal it is never left untreated In severe cases death may result from the effect of diphtheria toxin on the heart Ominous signs are pallor a rapid feeble pulse low blood pressure and cardiac irregularities such as extra systoles or various types of heart block The damage is reversible however and if the patient does recover he will have no permanent cardiac weakness

Peripheral nerve palsies are sometimes a late complication The commonest is palatal paresis which comes on 2 or 3 weeks after the initial throat infection and produces a nasal voice and a tendency for swallowed fluids to regurgitate through the nose Paralysis of ocular accommodation may occur about the same time and causes blurred vision Very rarely there may be weakness of the pharyngeal laryngeal or diaphragmatic muscles Widespread peripheral neuritis has been observed Recovery from all these nerve palsies is always complete

Diagnosis The diagnosis of ordinary faucial diphtheria is a clinical matter and the results of swabs are of secondary importance The chief points in clinical diagnosis are (1) the child looks ill more ill than the moderate temperature and mild throat inflammation would seem to warrant (2) the diphtheritic throat is not very painful and (3) the appearance of the membrane is usually characteristic

There are many other causes of sore throat but those which are most likely to be confused with diphtheria are acute streptococcal tonsillitis Vincent s angina and the sore throat of glandular fever In acute streptococcal tonsillitis the throat is very sore the fauces are acutely inflamed and the exudate if any is patchy soft and creamy in colour In Vincent s angina there is usually little constitutional disturbance and the patient seldom feels or looks really ill The throat though not very painful looks nasty it is often ulcerated and there is usually an extensive thick dirty greyish exudate or membrane Foetor oris is nearly always marked in contrast to diphtheria which has no smell The gums are often inflamed as well The faucial appearances in glandular fever can be very similar to those of diphtheria but there will usually be generalized glandular enlargement and a palpable spleen as well The blood count will be characteristic The throat of acute leukaemia may also be mistaken occasionally for diphtheria again the blood picture will be unmistakable

If diphtheria is suspected on clinical grounds a throat swab should certainly be taken to confirm the diagnosis Twenty four hours will elapse however before the result of the swab culture can be known If it is negative the clinical diagnosis is probably wrong but it is wise to repeat the swab in case there may have been a failure of technique If the result is positive and *C diphtheriae* are found in the culture this will confirm a clinical diagnosis of diphtheria It will not however upset a confident clinical judgment that the case is *not* diphtheria for the organism in the culture may well be an avirulent strain Tests for virulence take up to a week to carry out and are therefore of little help in the diagnosis of acute faucial diphtheria However they are of value when dealing with nasal or wound infections and in identifying carriers of virulent bacilli

Treatment. Diphtheria antitoxin is a specific remedy and the earlier it is given the better It can neutralize circulating toxin but toxin which has become fixed to tissue cells is beyond its reach If the clinical appearances suggest diphtheria antitoxin should be injected at once without waiting for the result of swabs When the membrane is confined to the tonsils an intramuscular dose of 30 000 units will be enough If however the membrane has spread to the palate or pharynx 100 000 units will be required half intramuscularly and the other half intravenously half an hour later Serum for intravenous administration should be warmed to body temperature and then given slowly Even with these precautions anaphylactoid reactions may occur and intravenous serum should not be given without adequate facilities at hand for treating such reactions (*see* p 68)

Penicillin should also be given 500 000 units intramuscularly every 12 hr will be adequate for the average patient Erythromycin is perhaps preferable in a severe case 250 mg is given by mouth every 6 hr Antibiotics are however of secondary importance compared to antitoxin

Because of the risk of toxic myocarditis diphtheria patients are best confined to bed and severe cases should be sent to hospital The general management differs in no way from that of the majority of severe infectious disorders (*see* p 72)

Laryngeal diphtheria though very rare nowadays is a serious complication If there are signs of respiratory obstruction tracheotomy should be done without delay

Nasal aural vaginal or wound diphtheria is seldom dangerous to the patient but may be a hazard to others 10 000 units of antitoxin will sometimes clear the infection rapidly if not erythromycin should be tried Such low grade chronic infections are however often difficult to eradicate and may require repeated therapeutic efforts during which time the patient must of necessity remain isolated

Prevention All children should be artificially actively immunized against diphtheria for only thus will the present day low level of morbidity and mortality be with certainty maintained Active immunization affords a high degree of protection It is possible to immunize a child simultaneously against diphtheria whooping cough and tetanus by giving a combined prophylactic (D T P P) the anti diphtheria constituent is purified toxoid 1 ml of D T P P should be injected into the deep subcutaneous tissues at the age of 3 or 4 months and two further similar injections given one 4 weeks and the other 8 weeks after the first Another 1 ml boosting dose will be required at the age of 1 year and a further one when the child starts school at 5 years old A final injection at the age of 9 or 10 completes the programme and the child will then in all probability be protected against diphtheria whooping cough and tetanus for life

Untoward reactions after such prophylactic toxoid inoculations are very rare in children but more common in adults For the active immunization of susceptible Schick positive adults it is therefore better to use toxoid antitoxin floccules (T A F) which though they give less lasting protection than purified toxoid are practically free from undesirable side effects A similar dosage scheme applies

Programmes of active immunization against diphtheria should be planned to take place during the

first half of the year in order to avoid the risk of precipitating paralytic poliomyelitis (*see* p 399)

Scarlet Fever

Scarlet fever or scarlatina results from infection by a strain of β haemolytic *Streptococcus pyogenes* which in addition to producing acute tonsillitis manufactures a so called erythrogenic toxin This toxin causes the characteristic skin rash There is no essential pathological difference between acute follicular streptococcal tonsillitis and scarlet fever and both are infectious Scarlet fever is however classed in Britain as a notifiable infectious disease whereas streptococcal tonsillitis is not The reason is that scarlet fever used to be a much more severe disorder but has undergone one of those spontaneous and mysterious changes of character that are so puzzling and fascinating to epidemiologists To day it is a mild transient infection hardly more troublesome than a common cold Whether it will always remain so or whether it will in time revert to its previously malign character is a question which only time will answer

The disease mainly attacks children under the age of 10 but infants are immune It is spread by droplet infection

Clinical Picture The incubation period varies from 2 to 7 days

The illness begins with the usual prodomal symptoms of an infectious fever (*see* p 70) and there is in addition a sore throat. The fauces are markedly inflamed and there may be spots or patches of creamy soft exudate on the tonsils The tongue at this stage is covered with white fur

The characteristic skin rash appears after 24 hr It consists of multiple punctate erythematous spots bright red in colour and can first be seen on the neck and thorax It then spreads rapidly over the whole body being particularly profuse in the limb flexures but usually absent from the area round the mouth A severe rash of this kind will last for 3 or 4 days but in the present day mild cases of scarlet fever the rash is often seen only on the trunk and may be gone again within 24 hr The sore throat usually clears up with the rash

The fur on the tongue thins and disappears as the rash develops and in a classical case of scarlet fever inflamed lingual papillae then give the tongue a strawberry appearance This is not often seen nowadays nor is the phenomenon of pin hole desquamation of the skin which used to follow a marked rash

Course and Complications Present day scarlet fever is a brief illness and all symptoms and signs have usually disappeared within 2 or 3 days Even without treatment uncomplicated cases almost invariably recover completely In the past however death from streptococcal toxaemia was not unknown

Complications are unlikely in a mild attack but the possibility of their occurrence makes treatment of scarlet fever still desirable The commonest is otitis media which can lead to mastoiditis meningitis cerebral abscess or lateral sinus thrombosis Sinusitis can also occur Two or three weeks after a severe attack of scarlet fever acute nephritis may develop as indeed it may do after any streptococcal infection However the routine use of antibiotics has greatly reduced the likelihood of this and other complications

Diagnosis Scarlet fever rarely presents any difficulty in diagnosis The association of a sore throat with a punctate erythematous rash which appears on the second day of illness is characteristic Occasional confusion may arise with similar rashes resulting from sensitivity to drugs like sulphonamides and barbiturates Such drug rashes however are seldom accompanied by tonsillitis

Throat swabs will often but not always succeed in demonstrating the presence of haemolytic streptococci

Treatment Patients should be kept in bed while pyrexial but unless the attack has been unusually severe can be allowed up as soon as the temperature is normal Little else is required in the way of general or symptomatic treatment

Penicillin should be given as a routine Not only does it minimize the risk of complications but it quickly gets rid of the streptococci in the throat and thus shortens the period of isolation About six days of treatment are required if the organisms are to be satisfactorily despatched Such a course of treatment is desirable even if the initial throat swab is negative for the streptococci are in fact almost certainly present At the end of the course a further swab should be taken If it shows no haemolytic streptococci the patient can be released from isolation If as occasionally happens the organisms are still present in the throat a few days of local treatment with penicillin lozenges will nearly always abolish them finally

The penicillin can be given intramuscularly but for children it is kinder and just as efficacious to give it by mouth Phenoxymethyl penicillin 125–250 mg every 4 hr is a suitable oral preparation

Whooping Cough

Whooping cough is endemic in Britain and there is a tendency to epidemics in alternate years It mainly attacks children under the age of 10 and is commonest during the winter months The causa

tive organism is *Haemophilus pertussis* which is highly infective but has low invasive powers Thus the infection nearly always remains localized to the respiratory tract and rarely spreads to other parts Whooping cough is acquired by the inhalation of droplets from patients in the early stages of illness or perhaps from unrecognized mild cases Symptomless carriers of infection are rare

Whooping cough is an important disease because it is one of the few acute bacterial infections that are little influenced by antibiotic therapy It can be dangerous to life when it occurs in infants and can also lead to permanent and crippling sequelae

Clinical Picture The incubation period is 10–14 days The onset is insidious with symptoms of a common cold Cough is at first mild but it increases in severity as the days pass until after about a fortnight it becomes severe and paroxysmal Typical spasms of coughing now occur many times a day each one consisting of a series of violent explosive expirations with little or no intervening inspiration The lungs are thus almost emptied of air and as a result the face becomes cyanosed and congested the veins stand out in the neck and the patient is extremely distressed At the end of the paroxysm there is a long crowing inspiration through the almost closed spastic glottis this is the characteristic whoop Vomiting frequently occurs immediately afterwards Thereafter the child often becomes quite normal and will go to sleep or play happily till the next paroxysm The bouts may be precipitated by excitement by the acts of eating or drinking or by other slight stimuli Infants sometimes do not whoop but simply have paroxysmal attacks of coughing or sneezing

Physical signs are few In the early catarrhal phase there may be scattered rhonchi and rales in the chest but in the paroxysmal phase there will usually be no detectable abnormality between the coughing spasms

Course and Complications. The paroxysms increase in severity for a few days then gradually decline and disappear during the next week or two Coughing may persist for several weeks longer but this is more due to habit than to continuing infection In most cases recovery is complete within six weeks of the onset

The disease is most dangerous to infants less than a year old and is rarely fatal after the age of 5 The most serious complication is bronchopneumonia the result of added infection with a streptococcus pneumococcus or *Haemophilus influenzae* Bronchopneumonia may supervene during either the catarrhal or the paroxysmal stage Next in order of gravity is meningo encephalitis which produces frequent severe fits Then again the violent bouts of coughing may cause mechanical trauma spontaneous pneumothorax subcutaneous emphysema hernia development intussusception and prolapse of the rectum have all been recorded Conjunctival haemorrhage is common but not serious cerebral haemorrhage rare but deadly Cerebral congestion without actual haemorrhage may be a cause of fits these are less frequent and less severe than the fits associated with meningo encephalitis but at the time it may be difficult to say which condition is causing them

Whooping cough is a common cause of serious bronchiectasis in later life What happens is that bronchi become plugged by sticky mucus with the result that segmental areas of pulmonary atelectasis develop Such areas of collapse are common during the course of whooping-cough but the majority re expand spontaneously Occasionally however the collapse is permanent and in such an event bronchiectasis inevitably develops in the atelectatic segment

Diagnosis Whooping cough is seldom correctly diagnosed during the early catarrhal phase unless there is a history of contact or an epidemic is on Indeed medical advice is often not sought until the whoop has appeared when of course diagnosis is easy The diagnosis may sometimes be missed in infants who do not develop a typical whoop but the paroxysmal nature of the bouts of coughing should arouse suspicion

The presence of *H pertussis* can if necessary be proved by using cough plates or by taking swabs from the naso pharynx The culture medium employed is defibrinated blood to which has been added some penicillin to discourage the growth of other organisms *H pertussis* is unaffected by penicillin In the cough plate method a Petri dish containing the culture medium is held about 6 in in front of the patient s mouth during a bout of coughing Positive results will nearly always be obtained during the catarrhal phase but less frequently in the whooping stage When the whoop has been present for a month cough plate cultures are usually negative

Blood counts will usually show a lymphocytosis after the whoop has developed The E S R is normal during an uncomplicated whooping phase if found to be raised at this time it indicates the presence of superadded infection

Chest X rays sometimes show enlargement of the mediastinal lymph glands but this finding is not constant enough to be of help in diagnosis

Treatment This can only be symptomatic as there is no specific remedy for whooping cough Claims have been made that chloramphenicol and

chlortetracycline (Aureomycin) are beneficial but there is little evidence to support them Antibiotics are therefore best kept in reserve for treating bronchopneumonic complications which are usually produced by more sensitive organisms

A child with whooping cough need not be kept in bed unless he looks ill but should be confined to the nursery and kept as quiet as possible Small doses of phenobarbitone 15–30 mg (¼ to ½ gr) twice or thrice daily according to age help to sedate him and to prevent coughing fits provoked by excitement Linctus amidone 0 5–1 ml (8–15 minims) is a useful cough suppressor The diet should be unrestricted indeed there may be difficulty in maintaining nutrition if post paroxysmal vomiting is frequent

During the catarrhal and early paroxysmal phases the child should be isolated both to prevent his spreading infection and to protect him from secondary invaders A month after the onset of the whoop he can be regarded as no longer infectious

Prevention A vaccine for artificial active immunization is available and is worth giving to all children even though the degree of protection it affords is not so great as that obtained by say diphtheria prophylaxis Whooping cough vaccine is usually combined with diphtheria and tetanus vaccines as D T P P of which 1 ml is the dose to be given by deep subcutaneous injection Three such injections at monthly intervals make up the primary course which is usually carried out between the ages of 3 and 6 months Further booster doses should be given at the ages of 1 year and 5 years Thereafter further whooping cough prophylaxis is unnecessary for the disease is rare and practically never fatal after the age of 5

B Those Acquired by Ingestion

Bacillary Dysentery

Organisms of the genus *Shigella* are responsible for the varieties of bacillary dysentery Shiga s bacillus is the most virulent and can produce fatal illness Flexner s bacillus is less toxic and Sonne s bacillus causes only mild disease

Dysentery is endemic in many countries and is particularly prevalent in tropical and subtropical zones Epidemics are common Shiga infection is fortunately rare in Britain Flexner infection does sometimes occur but the great majority of dysenteric outbreaks are caused by Sonne s organism Such outbreaks are common in schools hospitals and other institutions and mostly happen in the summer Infection is acquired by the ingestion of contaminated food or drink and the source is usually a mild unrecognized case of the disease or a convalescent carrier Permanent carriers are rare but dysentery organisms can sometimes persist in the bowel for a year or more after an attack Flies are frequently the vectors of infection between faeces and food

Bacillary dysentery used to be a great scourge of armies in the field but thanks to improved hygiene and methods of treatment was only a minor problem among the Allied troops in World War II

Clinical Picture Dysentery is an inflammation of the terminal ileum and colon which in severe cases may progress to ulceration The incubation period is from 2–7 days

The onset although it can be abrupt is more often gradual Mild cases have diarrhoea only Severe infections are accompanied by high fever nausea colicky abdominal pains tenesmus and profuse watery diarrhoea and usually reach their peak 2 or 3 days after the start There may then be as many as 30 or 40 watery motions a day faecal material is present at first but later the discharge becomes pure mucus mixed with blood

Course and Complications Patients with acute Shiga infection rapidly become very ill collapsed and dehydrated Untreated cases often die as the result of toxaemia and profound tissue electrolyte changes The profuse diarrhoea causes marked depletion of water and salt and a consequent clinical picture of profound weakness sunken cheeks and eyes dry tongue low blood pressure oliguria and muscular cramps

Flexner and Sonne infections are rarely fatal unless the patient is already enfeebled by some other condition The severity of the diarrhoea varies but recovery within a fortnight is usual Relapses are however not uncommon Bacillary dysentery rarely becomes chronic but a severe attack does sometimes leave behind it a tendency to colonic irritability and recurrent mild diarrhoea which may persist for months or years Such a syndrome is more likely to develop in patients who already because of achlorhydria or a nervous temperament or some other reason have a naturally loose bowel habit Repeated stool cultures in these people show no evidence of continuing dysenteric infection

Except in fulminating Shiga dysentery complications are rare However rectal prolapse arthritis polyneuritis iridocyclitis and parotitis are on record as occurring during severe attacks

Diagnosis There are no special features of the clinical picture of bacillary dysentery which distinguish it certainly from other acute bacterial diarrhoeas such as food poisoning or enteric fever and the diagnosis in sporadic cases usually depends

on the result of stool culture However when dealing with localized outbreaks among small communities in this country it is often possible to make a shrewd guess as to the type of infection if the features of the epidemic are observed Acute food poisoning is usually explosive in onset with many people sharply and simultaneously affected and the outbreak dies down rapidly in a few days Epidemics of Sonne dysentery come on more gradually with a progressive increase in the number of affected persons and may last several weeks

Sporadic mild cases have also to be distinguished from non infective causes of diarrhoea such as ulcerative colitis and malignant disease of the bowel In the former case stool culture is the deciding test.

Amoebic dysentery is rare in Britain and is seldom an acute disease Stool examination reveals the presence of *Entamoeba histolytica*

Treatment Bed rest is desirable for all but very mild attacks On theoretical grounds a residue free diet is often given uncooked fruit and vegetables cereals and porridge being avoided and cooked vegetables being puréed There is however no good evidence that such a diet favourably affects the course of the disease As the illness itself with its severe diarrhoea tends to cause malnutrition patients should be encouraged to eat plentifully Fluids should be given generously to avoid dehydration and in severe cases intravenous infusion of 5 per cent glucose in normal saline will be required

Morphine 10–16 mg (⅙–¼ gr) will relieve severe intestinal colic and rectal tenesmus In milder attacks Mist Cret Aromat. cum Opio B P C ½ oz 3 or 4 times daily will help to check the diarrhoea

Specific treatment with sulphonamides is usually effective The insoluble compounds such as succinylsulphathiazole and phthalylsulphathiazole are best They are poorly absorbed but break down to produce sulphathiazole in bacteriostatic concentration in the colon 3 g of succinylsulphathiazole or 1 5 g of phthalylsulphathiazole thrice daily are usually sufficient to check the disease

Although chloramphenicol and the tetracycline antibiotics are also active against dysentery bacilli they are liable to produce side effects and are therefore best kept for the treatment of persistent convalescent carriers in whom the organisms cannot be eradicated by sulphonamide therapy A persistent carrier state is particularly common after Sonne infections

Antiserum is available for fulminating Shiga infections 200 000 units are given intravenously and this dose can if necessary be repeated after 12 hr The value of this anti serum is however uncertain

Brucellosis

Brucellosis is also known as undulant fever or as relapsing fever because of its strong tendency to relapse It is primarily a disease of animals but is transmitted to man when he drinks infected raw milk *Br melitensis* affects goats and infected goats milk causes *Malta fever* in man *Br abortus* attacks cattle causing abortion and infected cows milk produces human *Abortus fever* *Br suis* which occurs in pigs rarely affects human beings

Malta fever and abortus fever are for practical purposes clinically identical The former is rare in Britain Abortus fever occurs mainly in country districts for the almost universal urban practice of milk pasteurization destroys the organisms

Clinical Picture The incubation period varies widely from 5 to 30 days The onset is insidious with increasing malaise headache vague aches in the back and limbs and pyrexia which slowly rises over several days to levels of 103 – 104 F There are seldom any localizing symptoms or signs and the clinical picture is one of subacute septicaemia The spleen and liver are sometimes palpable

Course and Complications Without treatment the disease pursues a chronic relapsing course with slow undulation of the temperature chart for months or even years Spontaneous recovery may eventually take place or death may follow prolonged wasting and toxaemia Endocarditis is a complication which often proves fatal Arthritis sometimes occurs in Malta fever but is rare in abortus infection Meningomyelitis has been described

Diagnosis The disease presents as a P U O and can seldom be diagnosed clinically except in countries like Malta where it is endemic Blood stool and urine cultures may be positive early in the illness but are not to be relied on and the diagnosis is usually made after the result of blood serum agglutination tests An agglutination titre of 1 100 is almost always found by the end of the second week of illness and thereafter the figure rises rapidly to 1 1 000 or even higher Such a rising titre is diagnostic However even a single reading of more than 1 200 is strongly suggestive of brucella infection The brucellin test consists of the intradermal injection of 0 1 ml of brucellin an antigen prepared from the organism It is positive if a local erythema appears 24–48 hr later However the brucellin test is like the Mantoux in that a positive result may only mean that infection has occurred in the past and is not necessarily an indication of current disease

Treatment General treatment consists of bed rest

and analgesics for the aching limbs The diet need not be restricted

The tetracycline antibiotics are effective against brucella oxytetracycline (Terramycin) being the drug of choice It is given orally in 250 mg doses *every 6 hr for a fortnight and usually brings the* temperature down to normal within a few days The patient should not however be dismissed prematurely for relapse within a week or two of stopping treatment is not uncommon Relapses which are seldom as severe as the original attack should be treated on similar lines with chlortetracycline (Aureomycin) or tetracycline (Achromycin) It is rare to get more than two relapses

Steps should always be taken to trace the bovine (or caprine) source of infection not only to prevent further human infection but also because unsuspected abortus infection in a dairy herd can mean the loss of many valuable calves

Enteric Fever

Enteric fever includes both *typhoid fever* and *paratyphoid fever* *The former is a severe septicaemic* illness caused by *Salmonella typhi* the latter a milder but similar disease produced by *Salmonella paratyphi* There are three types of *S paratyphi* A B and C Type B infection is the most prevalent enteric fever in Britain to day but even this is relatively rare Typhoid fever once a common urban scourge has been largely eliminated by efficient sanitation and hygiene

Patients with active disease convalescent carriers and healthy unwitting carriers are the reservoirs of enteric fever Organisms are discharged in the stools and urine and the disease is usually acquired by in*gestion of contaminated food or drink* Sewage contamination of water supplies was once a common reason for enteric fever outbreaks but now the source is usually a healthy carrier who works in a dairy food shop or restaurant History records a number of notorious carriers of this type 'Typhoid Mary (Mary Mallon) in the nineteenth century infected 8 out of 9 English families for whom she worked as a cook

Clinical Picture *The incubation period is from* 7 to 14 days Typhoid fever begins insidiously with headache malaise anorexia and a gradually rising temperature Epistaxis may occur constipation is common and there are sometimes shivering attacks By the end of the first week the temperature has risen to about 102 –103 F and there it remains while the patient steadily becomes more ill His pulse rate however remains relatively slow in comparison to the *high temperature* At this stage the spleen is usually palpable From the 7th day onwards rose spots appear on the skin These are small pink macules few in number and widely scattered each tending to disappear again after a day or two Successive crops of rose spots may appear for a week or more and are a characteristic feature of the enteric fevers They are however *easily overlooked*

Course and Complications During the third week of illness a patient with severe typhoid fever becomes desperately ill He is stuporose and *apathetic during the day delirious at night The* skin is dry and hot the tongue heavily furred the face sunken the eyes lack lustre the fingers like claws aimlessly plucking at the bedclothes This is the well known and oft described typhoid state Abdominal distension is often present and there may be profuse watery diarrhoea Typhoid attacks the Peyer s patches in the small gut producing inflammation and ulceration severe bleeding from the bowel may thus occur and occasionally an ulcer perforates causing peritonitis which is usually fatal An acute complicating haemolytic anaemia has also been described

If the patient avoids or survives these third week hazards the disease then subsides as gradually as it arose Recrudescences and relapses are not uncommon but are usually less severe than the original attack Chronic infection of the gall bladder and chronic osteitis are occasional sequelae

Paratyphoid fever is usually much less severe than typhoid The illness is shorter and is seldom fatal The clinical features are similar but toxaemia is relatively slight and bowel haemorrhage and perforation rarely happen Paratyphoid B the commonest enteric infection in Britain is sometimes so mild and transient that its nature goes unrecognized

Diagnosis In a classical attack of typhoid fever the combination of marked pyrexia relatively slow pulse rate palpable spleen and rose spots is unmistakable However many present day sporadic cases of mild typhoid and paratyphoid are not so easily identified at the bedside and often present simply as P U O In these mild illnesses diagnosis usually depends on the laboratory

Blood cultures are positive early in the attack but tend to become negative by the end of the second week The Widal blood serum antibody agglutination test may be positive in the first week and is invariably so by the third week Care is needed however in its interpretation as the following considerations will show

Salmonella organisms produce three antigens H O and Vi Each of these antigens can stimulate the production of a corresponding agglutinin H agglutinins are type specific that is from analysis of them it is possible to tell which particular sal

monella is present But they are of less value as indicators of current enteric disease because any one who has ever had the disease or active anti enteric immunization will always afterwards have H agglutinins in his blood Moreover in such a person any febrile illness is liable to cause a non specific increase in the H agglutinin titre (the anamnaestic reaction) Thus the finding of a high titre of H agglutinins in the blood of a pyrexial patient who has previously been inoculated against enteric fever is of little or no diagnostic value This is of some importance for most Britons who have served in the Armed Forces will have been inoculated

O and Vi agglutinins are less type specific but since they do not persist so long after anti enteric immunization as do the H agglutinins they are more useful in detecting active disease An O agglutinin titre of more than 1 50 usually means current enteric fever Vi agglutinins when they are present are equally indicative of active infection but they tend to disappear after the early stage of the attack Rising titres are diagnostic as indeed they are in all antibody detection tests Thus when faced with suspected enteric fever it is wise to perform a Widal test as soon as possible Even if the result of the first test is equivocal it will afford a baseline on which to judge the result of a second test taken a few days later A word of warning is necessary however Antibiotic treatment tends to interfere with normal antibody production A patient with enteric fever who is given antibiotics may not show the expected rise in agglutinin titre until late in the illness

Culture of the stools and urine will sometimes disclose the organism quite early in the illness and positive cultures are nearly always obtainable in the third week

During the active phase of illness a white blood cell count will in the absence of complications show a tendency to granulocytopenia and relative lymphocytosis Eosinophils often entirely disappear

Treatment Enteric fever though often mild is a potential killer and deserves to be taken seriously bed rest is necessary if the patient is at all ill Because of the tendency to enteritis it is usual to advise a light roughage free diet with soups pureed vegetables milk and egg dishes and sweetened fruit juice as the main constituents A generous fluid intake is desirable when there is marked pyrexia or a tendency to diarrhoea

Severe intestinal haemorrhage calls for morphine 10–16 mg (1/6–1/4 gr) and blood transfusion Perforation of the bowel is a grave complication though fortunately rare since the advent of antibiotic treatment surgical drainage of the p ritoneal cavity is usually advisable Extreme delirium may require morphine but central nervous depressants should if possible be avoided the mind is usually clouded enough as it is

For specific therapy the antibiotic of choice is chloramphenicol In the average case 500 mg orally every 6 hours will suffice but in severe attacks 3–4 g daily may be required The treatment should be continued for 10–14 days The blood count should be watched carefully and at any sign of severe leucopenia or of haemolytic anaemia the chloramphenicol should be stopped Relapses after antibiotic therapy are common for the drug delays antibody production They can however often be prevented by giving at the same time T A B vaccine 0 5 ml daily for 10 days

When the febrile phase of the illness is over there remains the problem of preventing a subsequent convalescent carrier state About 2 per cent of enteric fever patients become chronic faecal carriers who defy the repeated assaults of various antibiotics In most of them the organisms go to ground in the gall bladder where they may or may not produce symptoms of recurrent cholecystitis Cholecystectomy is often an effective cure Pure intestinal carriers and urinary tract carriers are rare

Chronic carriers are forbidden by law to engage in any trade connected with the handling of food and drink They should be carefully instructed in such measures of personal hygiene as will minimize the risk of their spreading disease

Prevention Good protection against enteric fever is afforded by active immunization with a combined typhoid paratyphoid vaccine (T A B) in which the organisms are killed either by heat or by alcohol 0 5 ml is given subcutaneously followed by 1 ml a fortnight later Some local reaction is almost invariable and a brisk general reaction with pyrexia not infrequent T A B immunity wanes rapidly and booster doses must be given yearly if it is to be maintained at a high level Members of the Armed Forces and other persons who are proceeding abroad to countries where enteric fever is more common than in Britain are inoculated with T A B as a routine The vaccine is often combined with tetanus toxoid (T A B T)

C Those Acquired by Inoculation

Anthrax

Anthrax is primarily a disease of sheep cattle horses and pigs and is caused by the *Bacillus anthracis* This is a spore bearing organism and the spores can survive in soil and other media for very long periods The disease can be acquired by people who work with animals or who deal with

animal hides and similar products However though the bacillus is a virulent one it is also of low infectivity for man and human anthrax is therefore a rare disease

Clinical Picture The incubation period is from 1 to 3 days The organism lodges in a small skin abrasion usually on the hand where it produces a vesicle surrounded by marked redness and oedema Further vesicles develop and later become pustular As the lesion spreads it becomes necrotic and a characteristic black crust forms at the centre At the same time there is enlargement of the local lymph glands together with fever and malaise

In woolsorters disease the organism is inhaled from infected wool or hides and produces a rapidly fatal broncho pneumonia The ingestion of infected meat may cause the symptoms of a severe bacillary dysentery

Course and Complications Anthrax can cause a rapid and fulminating septicaemia which may be fatal in a few days Mild skin cases which fortunately are much the most common usually recover but the rarer pulmonary and intestinal infections are deadly

Diagnosis Anthrax should be suspected when a vesiculated inflammatory skin lesion is found on anyone who handles animals or animal products An important point is that the lesion is not painful though the local glands are often tender If fluid is aspirated from the vesicle and examined microscopically anthrax bacilli will be seen

Pulmonary and intestinal forms of anthrax are often unrecognized but the severity of the illness and the occupation of the patient should arouse suspicion The bacillus can be identified in the sputum or faeces

Treatment The local skin lesion is best left alone Penicillin in full intramuscular doses (500 000 units every hr) or streptomycin (1 g every 12 hr) or both drugs together should be given Sclavo s anti serum is of doubtful efficacy but should be given in a desperate case in 50 ml intravenous doses every 12 or 24 hr for several days

Erysipelas

Erysipelas is a common infection of the skin and is caused by the β haemolytic *Streptococcus pyogenes* It is occasionally seen as a complication of wounds or of operation incisions but more often arises *de novo* on the face presumably as the result of inoculation through a small abrasion

Clinical Picture A red spot appears at the site of infection which is frequently on the bridge of the nose or on the cheek This rapidly enlarges to form an area of bright red brawny swollen tender skin with vesicles and bullae at its centre and a raised well defined margin There is marked pain and the temperature rises to 101 –103 F The local lymph glands are enlarged and tender

Course and Complications The swollen inflamed area may spread till it involves most of the face which becomes unrecognizable owing to the gross oedema of eyelids and lips However even while the wave of inflammation advances healing is taking place behind it in the original site of attack Eventually the infection subsides and recovery is usually complete within two or three weeks Erysipelas even if untreated is seldom dangerous to people in normal health but it is sometimes fatal in senile or enfeebled patients

Diagnosis The appearance of the erysipelas lesion is usually quite characteristic Herpes zoster on the face may produce vesiculation and inflammation but the red brawny spreading flare of erysipelas is absent Angio neurotic oedema or contact dermatitis may look rather like erysipelas but these conditions are not accompanied by high fever

Treatment Procaine penicillin 500 000 units every 12 hr will rapidly check the disease Equally good results are usually obtainable by oral sulphadimidine 0 5–1 g every 4 hr No local skin medication is necessary

Gonorrhoea

Gonorrhoea or vulgarly clap is a venereal disease caused by the *Neisseria gonorrhoeae* or *gonococcus* It is nearly always acquired by sexual intercourse with an infected partner but female children and occasionally adults may sometimes get it from contaminated towels clothing or lavatory seats The organism is present in the inflammatory discharge from the urogenital tract

In the male the disease attacks the urethra and neighbouring structures in the female the urethra the cervix uteri and other urogenital organs In both sexes septicaemic spread to distant parts of the body may occur though this is rare since the introduction of antibiotic therapy

Clinical Picture The incubation period is usually from 3 to 7 days

In the male the first symptom is a mild meatal irritation accompanied by a thin scanty urethral discharge Within a day or two the discharge becomes profuse and purulent there is discomfort on micturition and painful erections may occur Occasionally the symptoms are very mild and pass unnoticed In a severe case however there is obvious inflammation and swelling of the meatal orifice the anterior urethra is tender on palpation and periurethral abscesses may be felt The inguinal glands are often enlarged and tender

In the female the usual presenting symptom is a

purulent vaginal discharge but there may also be dysuria and frequency of micturition In a severe case the vulva is seen to be reddened and oedematous More often than in men however female gonorrhoea is mild and symptomless and is sometimes only diagnosed after a sexual partner has become infected

On vaginal examination the cervix uteri in an acute attack is seen to be swollen and inflamed and pus can be seen exuding from the uterine orifice Pressure on the urethra will often express purulent fluid from the meatus

The disease sometimes spreads in women to the rectum but the resulting proctitis is symptomless

Course and Complications *In the male* the average attack of gonorrhoea remains localized to the anterior urethra and gradually subsides without treatment The discharge becomes thinner less purulent intermittent and eventually after some weeks or months of this chronic *gleet* clears up

Not infrequently however the disease spreads after 2 or 3 weeks to the posterior urethra causing dysuria frequency of micturition and haematuria The prostate and seminal vesicles may then be involved and this will give rise to marked fever malaise perineal pain and severe dysuria The prostate is enlarged and extremely tender On rare occasions a prostatic abscess forms Usually the prostatitis clears up in time but sometimes a low grade infection persists for years Such chronic gonorrhoea infections however are unusual in males

Epididymitis is another common complication and sometimes a severe periurethral inflammation results eventually in urethral stricture

In the female spontaneous recovery may take place but chronic infection often ensues The disease lingers on in the cervix urethra or rectum with few symptoms or signs apart from a slight discharge but remaining a constant source of danger to others Persistent infection of Bartholin s glands is common

Occasionally the disease spreads to the uterine endometrium and to the uterine tubes Localized pelvic peritonitis may develop but general peritonitis is rare

Gonococcal septicaemia can occur in either sex but severe clinical septicaemia with such complications as endocarditis and pericarditis is a rare event More often a low grade blood borne infection manifests itself in the shape of iritis or of arthritis either in the acute or chronic phase of the disease Gonococcal arthritis (*see* p 527) is sometimes confined to a single joint but is more often polyarticular when it is clinically indistinguishable from a rheumatoid arthritis

Ophthalmia neonatorum is a gonococcal conjunctivitis which a new born child may acquire during its passage through an infected birth canal The inflammation is severe and if left untreated may result in corneal destruction and permanent blindness

Diagnosis Direct microscopic examination of stained films of the purulent discharge in acute gonorrhoea will nearly always demonstrate the presence of large numbers of gonococci In subsiding or chronic cases diagnosis is more difficult especially in the male for the organisms may be scanty and only intermittently present in a discharge which is often minimal Repeated cultures may eventually succeed in demonstrating them but often the diagnosis cannot be made with certainty until a small chronic focus of infection is run to earth Urethroscopy may demonstrate such a focus in one of Littré s glands or prostatic massage may succeed in expressing pus with gonococci in it from a small chronic prostatic abscess

A gonococcal complement fixation test (G C F T) on the blood serum is usually positive in chronic gonorrhoea but it is unwise to rely for diagnosis on this test alone False positive results are not infrequent moreover the test may remain positive for a time after the infection has died out The G C F T has perhaps most value in identifying the gonococcal origin of chronic phase iritis or arthritis when gonorrhoeal symptoms and signs are minimal or absent A positive result in such circumstances should lead to an intensive search for a cryptic genital focus of infection

In the male the chief condition which is likely to be confused with gonorrhoea is Reiter s disease This is a virus urethritis which is often associated with conjunctivitis and polyarthritis The disease follows a relapsing course for some months but eventually dies out Differential diagnosis largely depends on failure to demonstrate the presence of gonococci and on a negative G C F T

Staphylococcal and *E coli* infections of the urinary tract sometime produce a urethral discharge but cultures will readily identify the causal organism

In women *Trichomonas vaginalis* infection may cause confusion especially since it sometimes coexists with gonorrhoea

It should not be forgotten that syphilis can be acquired at the same time as gonorrhoea A Wassermann test on the blood should be done 3 months after the original gonoccoccal infection and repeated after a further 3 months

Treatment Acute gonorrhoea in the male responds well to penicillin and a single intramuscular injection of 300 000 units of procaine penicillin is

usually curative A second similar injection may occasionally be required Sulphathiazole or sulphadiazine 1 g every 4 hr by mouth for 5 days is almost as effective The patient remains ambulant

Complications such as acute epididymitis and prostatitis usually need rest in bed Procaine penicillin 600 000 units is given daily for 7 days Chronic prostatitis is treated by repeated prostatic massage by urethro vesical irrigations with 1 10 000 mercuric oxycyanide solution and by similar doses of penicillin Persistent infection of the anterior urethra and of Littré s glands may require urethroscopy and cauterization If a urethral stricture develops it will have to be progressively dilated with urethral sounds Instrumental treatment of this kind is a matter for a specialist

Women with acute gonorrhoea should be kept in bed and given 300 000 units of procaine penicillin daily for 3 or 4 days Acute pelvic complications should be treated conservatively with full doses of soluble penicillin unless a tubal abscess forms or general peritonitis supervenes when surgery may be required

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Ophthalmia neonatorum can be aborted if penicillin drops (10 000 units in each ml) are put in the baby s eyes at the time of delivery

Gonococcal vulvo vaginitis in little girls is often very persistent and may require several courses of penicillin to cure it

Gonococcal arthritis is treated on the same general lines as rheumatoid arthritis (*see* p 512) In addition any chronic focus of gonorrhoeal infection must be hunted down and dealt with The same applies to iritis

In treating gonorrhoea it is not enough to render the patient symptom free the disease must be entirely eradicated otherwise it remains a constant source of potential danger to a sexual partner Cure is not complete until there is no discharge a normal urine and cultures of urethral prostatic or vaginal secretions are repeatedly negative

Tetanus

Tetanus or lockjaw is the result of infection with *Clostridium tetani* an anaerobic spore bearing bacillus whose normal habitat is the bowels of horses and sheep Tetanus spores lurk in soil and horse manure being tough and able to survive in such media for years Infection occurs when a wound or skin abrasion is contaminated by spore containing soil and no age is immune The organism being an anaerobe develops best in the depths of deep and dirty punctured wounds especially if there is necrosis of tissue due perhaps to the presence of deeply-embedded splinters or shell fragments The disease is therefore most likely to arise after war wounds or road accidents Occasionally however the site of entry of the organism may be very small and insignificant and in such circumstances the disease seems to arise without preceding trauma

Cl tetani do not spread beyond the site of inoculation but produce a deadly exotoxin which travels up the nerves to reach the spinal cord and brain

Clinical Picture The average incubation period is between 7 and 14 days but it may be as short as 3 days or as long as 3 weeks The shorter the incubation period the more severe the attack

The first symptom of generalized tetanus is a slight stiffness in the jaw (trismus) and neck muscles The mouth cannot be opened as widely as usual and swallowing becomes difficult The muscular spasms spread with varying rapidity to the trunk and limbs producing eventually the classical clinical picture of tetanus with its snarling grin (risus sardonicus) arched back (opisthotonus) tense indrawn abdomen and extended rigid limbs On top of this constant spasm are superimposed sudden repeated attacks of hyper rigidity when the whole body is thrown into a fearful tonic contraction during which muscles may rupture and bones be broken These attacks are precipitated by any slight stimulus and are intensely painful A distressing feature of the disease is that the patient s mind remains clear almost till the point of death The illness is often apyrexial throughout

Localized tetanus a much milder illness in which the spasm remains localized to muscles near the site of injury and infection is met with in patients who are partially protected as the result of inadequate passive immunization or who have been actively immunized in the past but have not continued with regular refresher doses

Cephalic tetanus is a rare variety which sometimes follows injuries to the head only the face and pharyngeal muscles are involved

Course and Complications About half the patients with generalized tetanus die from exhaustion after a week Recent methods of treatment however may lower this figure In those cases that recover the spasm and attacks of hyper rigidity lessen in severity and finally disappear Throughout

the acute phase however there is an ever present risk of respiratory infection The muscular spasm interferes with breathing and with swallowing and as there is also excessive pharyngeal and tracheo bronchial secretion aspiration pneumonia and pul monary collapse are common and often fatal complications

Localized tetanus has a low mortality cephalic tetanus a very high one

A good guide to prognosis is the length of the interval between the onset of trismus and the first occurrence of a generalized tonic convulsion If this is less than 48 hr the outlook is grave indeed The longer it is the better are the prospects of recovery

Diagnosis Tetanus at the time of onset has to be distinguished from other causes of trismus such as infections of the teeth and throat In these conditions however the neck muscles are seldom affected When fully developed the clinical picture of tetanus is unmistakable Strychnine poisoning causes repeated muscular cramps but between attacks the muscles relax completely In hydro phobia a disease almost unknown in Britain simi lar spasms are provoked by the sight of water or by attempts to drink but again there is no inter vening rigidity Hydrophobia also produces marked mental changes Acute meningitis may occasionally cause such severe rigidity of the neck and back as to mimic tetanus The cerebro spinal fluid will how ever be abnormal whereas in tetanus it is un changed

Occasionally the fear of lockjaw may produce hysterical trismus in a wounded man but the illness does not of course develop any further

Treatment It is doubtful whether anti tetanus serum (A T S) is of much value in *established* tetanus for once the toxin has reached the central nervous system it is fixed and is no longer capable of being neutralized by antitoxin However it is possible that even after symptoms have appeared there may still be some free toxin in the tissues round the wound and it is therefore advised that a single dose of 200 000 units be given intra venously as soon as possible after the diagnosis has been made

The patient should be in bed in a quiet darkened room in hospital Every effort must be made to avoid noise and other stimuli Oral feeding is best avoided because of the difficulty in swallowing and risk of aspiration pneumonia nutrition and fluid balance are maintained by continuous intravenous infusions Heavy sedation will be required The drug of choice is chlorpromazine 0 05 to 0 15 g intramuscularly or intravenously every 4 to 6 hr Tracheostomy with tracheal intubation is indicated when pharyngeal secretion is profuse and there is difficulty in maintaining a clear airway

Procaine penicillin 600 000 units every 12 hr should be given to combat any wound sepsis and to prevent respiratory infection Larger doses will be necessary if pneumonia develops The wound itself should be given only essential immediate surgi cal treatment and then left alone until the tetanus is better

Prevention Active immunization can be achieved by means of tetanus toxoid and should begin in childhood The toxoid is usually combined with diphtheria and whooping-cough prophylactics and the initial course consists of three 1 ml doses of the mixture (D T P P) at intervals of 4 weeks The prophylactic is injected into the deep subcutaneous tissues This initial course is given during the first 6 months of life and a further 1 ml dose a year later will produce a high level of immunity to tetanus To maintain this high level it is necessary to repeat the injections about every 12 months but even if this somewhat strenuous programme is not carried out a reasonable partial immunity will result from the original course and will probably be sufficient to ensure that any attack of tetanus in later life will be fairly mild and non fatal Curiously enough an attack of the disease itself gives only temporary immunity and second attacks are possible though unusual

Most members of the British Armed Forces are actively immunized while serving the toxoid being as a rule combined with anti enteric vaccine in T A B T Two 1 ml doses are given at an interval of 4–6 weeks and these are followed by regular 1 ml booster injections

Whatever view may be taken of the usefulness of A T S in the treatment of established tetanus there can be little doubt of its value in aborting early infection The routine administration of A T S to all seriously wounded casualties has made tetanus to-day a rare disease Unless the individual is known to have been actively immunized recently he should be given a subcutaneous injection of 3 000 units of A T S as soon as possible after the injury and indeed it is wise to give it even to an actively immunized man if his wound is deep and dirty The giving of A T S does of course carry a risk of subsequent serum sickness and more serious a very small chance of an immediate anaphylactoid reaction (*see* p 68) In theory the risk can be avoided in actively immunized casualties by giving them instead a booster dose of tetanus toxoid which is free from side effects But it must be re membered that full immunological response to such a booster dose takes up to 5 days to develop This does not matter much in civilian practice for the

usually curative A second similar injection may occasionally be required Sulphathiazole or sulphadiazine 1 g every 4 hr by mouth for 5 days is almost as effective The patient remains ambulant

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degree of respiratory tract inflammation and a pyrexial illness which starts suddenly is attended by marked prostration considerable muscular pains and evidence of respiratory infection is quite likely to be influenza There is no doubt however that influenza tends to be an overworked diagnostic label indeed it has with some truth been said that it is the refuge of the diagnostically destitute Non paralytic poliomyelitis primary tuberculous infection virus pneumonia Q fever and atypical attacks of specific fevers often get labelled influenza Sporadic influenza is not a very common disease to diagnose it frequently in the absence of an epidemic marks a physician as either lazy or incompetent Incidentally the lay man s flu is usually not influenza but simply a heavy cold

Treatment There is no specific treatment for uncomplicated influenza and the general measures outlined on p 72 are appropriate Aspirin analgesics are usually required for the headache and muscular pains and hypnotics may be necessary for insomnia Inhalations of steam will ease a painful tracheitis

Bronchopneumonia due to secondary invaders is treated as on p 338 Coccal infections respond to sulphonamides and penicillin The *Haemophilus influenzae* is resistant to penicillin but sensitive to streptomycin and the tetracyclines

An attack of influenza confers only transient immunity and repeated attacks can occur

Prevention Considerable research has been devoted to the problem of providing a suitable anti influenza vaccine but the existence of many influenza viruses and variations in the antigenic properties of individual viruses make matters difficult So far no generally useful prophylactic has been developed

Measles

Measles or morbilli is a mild disease but its complications are occasionally dangerous It is endemic in most parts of the globe and tends to become epidemic in cities during the winter months In Britain epidemics are inclined to occur in alternate years Children under the age of 5 are chiefly affected Infants below the age of 6 months are usually immune owing to the persistence of anti bodies derived *in utero* from the mother The disease is spread by droplet infection

Clinical Picture The incubation period is about 14 days Measles begins with the symptoms of a feverish cold and then goes on to bronchitis There is also some conjunctivitis and photophobia and the child with its reddened running eyes and nose looks and feels thoroughly miserable At this stage examination of the buccal mucosa will reveal the presence of minute discrete white spots each surrounded by a bright red flare chiefly congregated on the inside of the cheeks round the parotid papillae and opposite the premolar teeth These are Koplik s spots and are characteristic of the disease

After 3 days the catarrhal symptoms subside the temperature falls temporarily and the Koplik s spots begin to fade Then on the fourth day of the illness the temperature rises again and the skin rash appears This is a blotchy macular eruption purplish red in colour which begins on the fore head and behind the ears and later spreads to the face trunk and limbs The elements of the rash are of all sizes from small spots to large irregular confluent areas

When after a day or two the rash has fully developed the patient feels much better

Course and Complications After a week of illness the rash begins to fade and the temperature to fall Recovery is usually rapid

Complications due to secondary bacterial infection are common bronchopneumonia segmental pulmonary atelectasis otitis media and keratitis may occur On rare occasions the virus itself can cause encephalitis This is a serious complication with a 30 per cent mortality and a distinct risk of permanent mental incapacity

Diagnosis In a typical attack this is easy the Koplik s spots and the skin rash are highly characteristic Mild attacks are sometimes mistaken for rubella but the error is not very important unless the patient is a pregnant woman (*see* p 90) Rashes due to drug sensitivity are sometimes morbilliform but they are as a rule unattended by catarrhal symptoms and any accompanying pyrexia is usually transient

Leucopenia is often found at the height of the illness if no complications have developed

Treatment There is no specific treatment for uncomplicated measles and the general measures outlined on p 72 are appropriate Bacterial complications should be treated with sulphonamides or antibiotics but these are ineffective in measles encephalitis

Prevention Measles can be dangerous to invalids or to small weakly children and these if they become contacts should be passively protected by gamma globulin The protection lasts 2 or 3 weeks which is long enough to prevent an attack from developing Even if the attack is not entirely checked it will be rendered mild For a child under 3 years old an adequate dose of gamma globulin is 750 mg given intramuscularly as soon as possible after the contact

interval between injury and injection of toxoid is likely to be short but in war time there may well be considerable delay and thus the antibodies produced in response to the toxoid may not be developed in time to combat the infection successfully The rule is when in doubt give A T S

Virus Diseases

A Those Acquired by Inhalation

Influenza

Influenza or grippe is a highly infectious acute illness which results from invasion by one or more members of a group of viruses Of these influenza viruses types A and B are clinically the most important Virus A has been responsible for most of the major influenza epidemics in the past virus B for some less severe outbreaks Other members of the group may account for sporadic cases or for some minor epidemics However the question of virus type aetiology in influenza is still being investigated

Influenza is an ancient disease and was probably the sweating sickness of medieval times It is endemic is most countries and tends to become epidemic in the winter months In the last 100 years there have been three world wide pandemics and the last of these in 1918–1919 was one of the worst plagues that mankind has experienced over twenty million people died Fortunately influenza of such virulence has not been seen since

The disease is spread by droplet infection and no age is immune The virus chiefly attacks the respiratory tract and has a peculiarly destructive effect on the ciliated epithelium of the trachea and bronchi It is probable that the removal of this important natural barrier to infection explains why influenza has such a markedly lowering effect on the patient s resistance to other organisms Secondary invasion by streptococci staphylococci pneumococci and *Haemophilus influenzae* (so named because it was originally believed to be the cause of influenza) is common and it is this secondary invasion rather than the original infection which constitutes the main risk of present day influenza

Clinical Picture The incubation period is 1–3 days The onset is abrupt with early marked pyrexia The symptoms are protean and vary a good deal in different epidemics In some respiratory symptoms predominate there is rhinitis pharyngitis substernal aching due to tracheitis and a paroxysmal cough The throat is reddened though there is no exudate and the lungs are full of râles and rhonchi In other epidemics respiratory symptoms are slight and the chief features are vomiting abdominal pain and diarrhoea Sometimes the brunt of the attack falls on the central nervous system and there is severe headache backache and insomnia without however marked neck stiffness

In every severe attack of influenza there is considerable malaise and prostration with widespread muscular pains Sweating is often profuse the pulse rate is slow in relation to the height of the temperature and there is a tendency to hypotension Patients with pronounced respiratory symptoms frequently are slightly cyanosed and in the pandemic of 1918–1919 a peculiar heliotrope facial colour was seen in the worst cases

Course and Complications Uncomplicated attacks of influenza usually recover spontaneously The fever abates slowly after a week but relapses are not uncommon Persistent depression and debility with a tendency to hypotension are common in the convalescent stage which therefore tends to be prolonged Effort syndrome (*see* p 290) may arise in predisposed individuals and psychological depressions are sometimes precipitated by an attack of influenza

The commonest and most serious complication is bronchopneumonia which has in past epidemics accounted for most of the deaths It is as a rule caused by secondary coccal invasion but *Haemophilus influenzae* is sometimes to blame or the infection may be a mixed one Sinusitis and otitis media are also common complications and encephalitis arthritis pericarditis myositis and orchitis have been described However it is possible that some of the cases reported with these rarer complications were not true influenza

The disease leaves behind it no permanent sequelae

Diagnosis This is usually made on clinical evidence for although culture of the virus from nasal or pharyngeal washings is possible and a specific agglutination inhibition test exists technical difficulties make it impossible to use these procedures as a routine The disease is unaccompanied by any important changes in the blood cerebro spinal fluid or urine

Clinical diagnosis of a disorder with such diverse manifestations must always be difficult and in sporadic cases can often be made only by exclusion of other conditions During epidemics the task is easier A list of differential diagnoses for influenza would include nearly every infectious disease However most attacks are accompanied by some

degree of respiratory tract inflammation and a pyrexial illness which starts suddenly is attended by marked prostration considerable muscular pains and evidence of respiratory infection is quite likely to be influenza There is no doubt however that influenza tends to be an overworked diagnostic label indeed it has with some truth been said that it is the refuge of the diagnostically destitute Non paralytic poliomyelitis primary tuberculous infection virus pneumonia Q fever and atypical attacks of specific fevers often get labelled influenza Sporadic influenza is not a very common disease to diagnose it frequently in the absence of an epidemic marks a physician as either lazy or incompetent Incidentally the lay man s flu is usually not influenza but simply a heavy cold

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Healthy older children should be allowed to develop the disease, for the immunity conferred is solid and second attacks are rare

Isolation of measles cases will be ineffective in preventing spread of infection unless it is carried out in the early catarrhal phase Infectivity is then at its height but is much less by the time the skin rash appears

Mumps

Mumps or epidemic parotitis is a highly infectious disease which is spread by droplet infection and which attacks school children and young adults It is a trivial disorder in children but adults can be quite ill Babies under 6 months old are immune Mumps is endemic in most civilized countries and small localized epidemics in the spring months are common

Clinical Picture The incubation period is about 21 days The first symptoms are those of a mild feverish cold followed very soon by painful tender swelling of one or both parotid glands The submaxillary and sublingual glands may also be involved In children the constitutional disturbance is usually slight but adults often have marked pyrexia and malaise

Course and Complications The salivary gland inflammation subsides in a week or 10 days leaving behind no permanent ill effects Complications are rare in children and death from mumps is very uncommon The disease confers lasting immunity and second attacks are unusual

The most serious complication is orchitis in adult males for this may be followed by permanent atrophy of the affected testicle Fortunately orchitis is rarely bilateral When it occurs usually about a week after the onset of parotitis the testicle becomes swollen and acutely tender and a hydrocele may develop Rarely acute orchitis may be the only overt symptom of an attack of mumps this applies also to other complications Oophoritis sometimes occurs in adult women but atrophy of the ovary never follows This is because the ovary in contrast to the testicle is not enclosed in a thick inelastic fibrous tunica Inflammatory swelling can thus occur without restraint The swollen testicle on the other hand is constricted by its covering and is thus liable to ischaemic damage

Acute pancreatitis is a rare complication though alarming at the time it always recovers spontaneously Meningoencephalitis may like orchitis supervene after about a week of illness and results in severe headache clouding of consciousness and delirium Peripheral neuritis is sometimes seen and may attack the cranial nerves The optic facial and auditory nerves are most frequently involved and permanent nerve deafness is an occasional sequel However in most cases the neurological complications of mumps clear up without permanent damage Acute mastitis has been described

Diagnosis Except in those rare cases that are unaccompanied by parotitis diagnosis is seldom difficult for few acute illnesses are associated with swelling of the parotids Acute suppurative bacterial parotitis is seldom seen except as a terminal event in some severe illness such as typhoid fever or uraemia A salivary duct calculus can produce acute enlargement of the gland but the swelling is usually transient recurrent and characteristically provoked by the sight and taste of food Other causes of parotid enlargement are chronic diseases unlikely to cause diagnostic confusion

During the acute stage of mumps there is usually a relative lymphocytosis and a complicating meningoencephalitis is attended by a lymphocytosis in the cerebro spinal fluid

There is a complement fixation blood test but it is rarely required except to detect subclinical or atypical infections

Treatment. There is no specific treatment for the disease but analgesics are desirable for the relief of pain Complications can be treated only symptomatically Pancreatitis and oophoritis do not require surgical intervention

In a child rest in bed is only necessary while the temperature is raised The patient is probably infectious until the glandular swelling has subsided

Rubella

Rubella or German measles is an extremely mild disease whose only importance lies in the fact that when it occurs in a pregnant woman it may damage the foetus It is endemic in most countries and small localized epidemics are common during the spring months Large outbreaks are rare School children and adolescents are chiefly attacked The disease is spread by droplet infection

Clinical Picture The incubation period is usually about 14 days but may be rather longer Sometimes there are some mild catarrhal symptoms at the onset but often the skin rash is the first noticeable feature It appears on the second day of illness and consists of pink macules of varying size These are first seen on the face but soon spread to the trunk and limbs They fade rapidly and are usually gone in 2 or 3 days With the rash there is enlargement of some groups of lymph glands the suboccipital and cervical glands are most commonly affected but epitrochlear and popliteal groups may also be involved

Course and Complications Rubella is never fatal and in most cases is so mild and fleeting a disorder

that the patient is hardly disturbed Adults some times have some pyrexia and constitutional upset

When the disease occurs during the first 4 months of pregnancy it is peculiarly liable to cause foetal damage and the child may be born subsequently with serious ocular aural dental cerebral or cardiac defects Estimates of the degree of risk vary but all agree that it is considerable Indeed many obstetricians regard the occurrence of rubella during early pregnancy as an indication for artificial termination When the disease happens after the fourth month however the likelihood of foetal injury is very much less and the pregnancy can be allowed to continue

Other complications of rubella are extremely rare

Diagnosis Rubella may be mistaken for measles scarlet fever or glandular fever The measles rash is rather similar but in measles the catarrhal symptoms are more prominent Koplik s spots are present in the mouth and there is no lymph gland enlargement The mild scarlet fever of the present day sometimes mimics rubella but the presence of a sore throat and the limitation of glandular enlargement to the tonsillar glands should help in its differentiation In any case unless the patient is pregnant it is not of great practical importance to distinguish between two such mild infections When glandular fever produces a skin rash it is often very like that of rubella but in glandular fever there will usually be marked lymphocytosis whereas in rubella there tends to be leucopenia with a relative increase in the numbers of Turck and plasma cells Moreover in glandular fever the Paul Bunnell test is usually positive

Treatment Rubella seldom requires any treatment and bed rest is only necessary for adults who are ill with it Infectivity disappears with the rash

Women in the early months of pregnancy who come into contact with the disease should be protected by being given 1 5 g of gamma globulin intramuscularly as soon as possible after the contact On the other hand no attempt should be made to check the spread of small epidemics in girls schools The more children that get it the better for the immunity produced by an attack is solid and long lasting

Chicken Pox

Chicken pox or varicella is a mild but highly infectious disease which is spread by droplet infection and which chiefly attacks school children It is endemic in most countries and localized outbreaks in schools and institutions are common during the autumn and winter months The causal virus is closely related to if not in fact identical with the virus that causes herpes zoster Children who come into contact with patients suffering from herpes zoster not infrequently develop chicken pox as a result

Clinical Picture The incubation period is 14 to 21 days Children with chicken pox are usually little disturbed by it and in them the skin rash is often the only clinical feature Adults however usually display some prodromal symptoms of head ache malaise and pyrexia for 2 or 3 days before the rash appears Sometimes a transient erythematous rash like that of scarlet fever precedes the true chicken pox rash it is not accompanied by any sore throat

The true rash consists of numerous reddish papules which rapidly turn into oval vesicles and then owing to secondary infection by skin organisms into pustules After a time the pustules rupture and the lesions scab over dry up and finally disappear Characteristically during the first 3 or 4 days of the disease successive crops of papules appear and evolve so that at any given time it is possible to see papules vesicles and pustules side by side The general distribution of the rash is centripetal that is the lesions are more numerous on the trunk sparser on the face and limbs and relatively scarce on the extremities They can often be seen in the axillae and may appear in the mouth and pharynx

Course and Complications Most cases of juvenile chicken pox run a mild afebrile course the lesions disappearing after a week or two As however the rash itches scratching may lead to secondary infection and consequent delay in resolution It is rare for permanent scarring to follow

Complications are rare Encephalitis has been described but always recovers spontaneously

Diagnosis This is not difficult in a typical case the type and distribution of the skin lesions being characteristic It is important however not to mistake mild smallpox for chicken pox the differential points are discussed on p 92

Papular urticaria may produce lesions rather like those of chicken pox but there is no particular tendency to a centripetal distribution the rash rarely invades the face and is never seen in the mouth

The lesions of scabies are more irritating and characteristic mite burrows are to be seen between the fingers and toes

Treatment The average case of chicken pox needs no treatment and the patient need not be confined to bed A soothing dusting powder such as Lactocalamine will allay pruritus Secondarily infected lesions may need the local application of sulphonamide or penicillin ointments

Smallpox

Smallpox or variola is an ancient and dread disease which at one time used to ravage most parts of the world Widespread epidemics were common and in 1870–1874 when the last major outbreak occurred in Britain 42 000 people died Since then mass vaccination has more or less banished the severe *variola major* from most civilized communities but it is still fairly common in Egypt and India A mild variety *variola minor* or *alastrim* appears now and again in the Western Hemisphere

Although smallpox is rare in Britain to day many epidemiologists feel uneasy about the situation The present low rate of infant vaccination means that a large part of the population is unprotected so that future epidemics of smallpox are again a serious possibility It is therefore important to be *able to recognize the disease quickly in order that* immediate steps can be taken to isolate sufferers and to trace and vaccinate contacts The disease is highly infectious and is spread by droplet infection Air travel has greatly increased the risk of smallpox being introduced into this country Formerly a traveller who had picked up the disease in the East would develop overt symptoms on the sea voyage and would therefore be isolated and treated before his arrival in Britain Nowadays he may get here by air within the incubation period and thus spread infection before being recognized

Clinical Picture The incubation period is between 10 and 15 days The illness begins with headache backache vomiting and marked pyrexia and these prodomal symptoms are usually present for 2 or 3 days before the characteristic skin rash appears Occasionally during this period there may be transient erythematous or petechial rashes On the third day of illness pink macules appear which *gradually change into papules then to round* vesicles and finally to pustules the time taken for each macule to become a pustule being about a week With the onset of the true rash the temperature usually falls but it rises again to reach a peak at the stage when the lesions become pustular

The macules appear first on the face then spread to the arms and trunk and later to the feet There is none of the repeated cropping such as occurs in chicken pox and at any given time all the skin lesions in a particular part of the body will be at the same stage of development The rash tends to be *centrifugal* in distribution that is it is sparse on the trunk and profuse on the upper part of the face on the forearms and on the feet and lower parts of the legs Lesions are thus particularly common on the more exposed parts of the body and are rare in sheltered situations like the armpits They are often seen however inside the mouth and pharynx

Course and Complications At the pustular stage of the rash about ten days after the onset the patient with severe smallpox becomes extremely ill with marked toxaemia and delirium Death may occur at this point in the old style epidemics of variola major the mortality was about 25 per cent. However in variola minor death is unusual and now there begins a slow decline in the temperature and a gradual improvement in the patient s state The pustules break down become scabbed over and dry up Convalescence is slow as the crusted lesions may take many weeks to separate and disappear Permanent scarring or pock marking was common in the past but it was usually due to severe secondary infection of the lesions and has been rare since antibiotics have been used to prevent this

Haemorrhagic and confluent smallpox are particularly severe and fatal varieties of variola major but are rarely seen except in countries where the major disease is endemic On the other hand *varioloid* is the name given to an extremely mild type of illness which is sometimes seen in individuals who have been vaccinated years before and who therefore have a waning but still appreciable degree of partial immunity In such cases the lesions may be few and scattered and the constitutional upset very slight The danger of varioloid is that it is easily missed and yet patients with it are just as capable of spreading infection as those with more florid disease

Encephalitis is an occasional complication Secondary bacterial invasion may give rise to bronchopneumonia conjunctivitis otitis media orchitis and severe pustular dermatitis

Diagnosis Smallpox should always be thought of when spots occur in anyone who has recently arrived in Britain from the Middle or Far East It should also be borne in mind if the patient lives near the docks in a sea port A history of vaccination within the previous 12 months excludes the possibility of smallpox provided there is good reason to believe that the vaccination took but evidence of more remote or of unsuccessful vaccination carries no such guarantee of immunity

Clinical diagnosis is not difficult in a classical case of variola major but variola minor and varioloid are easily missed or may be taken for chicken pox Points to which particular attention should be paid are the centrifugal distribution of the rash *its* preference for exposed convex skin areas and avoidance of sheltered concavities the frequent presence of lesions in the mouth and pharynx and the evidence of an orderly and uniform progression

of the lesions from macule to pustule The chicken pox rash is centripetal in distribution and prefers sheltered to exposed areas of skin moreover the successive cropping of the lesions results in the presence of macules papules vesicles and pustules all together in any given situation

Other papulo vesicular rashes which may mimic smallpox include those due to secondary syphilis papular urticaria erythema multiforme dermatitis herpetiformis secondarily infected scabies the Stevens Johnson syndrome and to drugs like bro mides and iodides None of them has the charac teristic smallpox distribution however nor do the lesions progress in the orderly way of smallpox There is little likelihood that such conditions would be thought to be smallpox the risk is of the oppo site error If there is any suspicion of variola the patient should be at once isolated in hospital and the public health authorities notified without delay Hospitals and local authorities in all parts of Britain have a list of experts with special experience of smallpox abroad who are available for imme diate consultation

Laboratory methods of diagnosis include the microscopic examination of scrapings from papules or vesicles for the typical inclusion bodies of the smallpox virus and the culture of such material on the chorio allantoic membrane of a hen s egg A complement fixation test can be applied to a saline extract of such scrapings These methods are reliable and will provide an answer within 24 or 48 hr but they demand a suitably equipped labora tory and expert technical skill

Treatment. There is no specific treatment for smallpox Severe cases will require skilled nursing with particular attention to those lesions in the mouth and near the eyes A 0 001 per cent aqueous solution of potassium permanganate can be used to clean the skin lesions Phenoxymethyl penicillin (Penicillin V) 125 mg should be given every 4 hr by mouth to prevent secondary infection

The highly infectious nature of smallpox is well known though the widely held belief that the virus can travel in air currents over a considerable dis tance is probably erroneous Nevertheless strict iso lation of patients in hospital is essential and their attendants must observe rigorous antiseptic pre cautions and be themselves fully protected by vaccination Thorough disinfection of the patient s clothing of his house and its contents and of ambulances hospital bedding and furniture will be required Contacts must be traced vaccinated and kept under medical supervision for at least a fortnight

Prevention The prevention of smallpox by vac cination is described below

B Those Acquired by Inoculation

Vaccinia

The virus of vaccinia is the same as that of smallpox but its virulence has been modified by passage through a cow in which it produces cow pox After such passage it is no longer capable of causing severe disease in human beings but is still fully capable of stimulating the production of anti bodies Human infection with vaccinia virus is occasionally in farm hands and dairy maids ac quired accidentally by inoculation from cattle with cowpox but is of course more often deliberately induced as a protection against the unmodified smallpox virus Vaccination was originally intro duced in 1796 by Edward Jenner who observed that milkmaids who had had cowpox never got small pox The present day technique is to inoculate the recipient s skin with a glycerin and saline suspen sion of the material from the vesicles on the hide of a calf with cowpox the susp nsion is referred to as calf lymph

The immunity produced by vaccination depends to some extent on the technique employed but probably remains high for 3 or 4 years and declines thereafter To maintain immunity re vaccination at intervals is therefore necessary and in a country where smallpox is endemic should be done every 5 years In Britain however a practical plan is to vaccinate babies at the age of 3 months to re vaccinate at the school entry age of 5 years and finally at the school leaving age of 15 years Such a programme will ensure that the subject will have at least partial immunity more or less indefinitely and that any subsequent attacks of smallpox will almost certainly be mild Nevertheless anyone who comes into contact with smallpox should unless he has been vaccinated within the previous 12 months be re vaccinated immediately Doctors and nurses in hospital isolation units who may have to deal with smallpox patients should be vaccinated regu larly every 5 years

Vaccination is a *sine qua non* before travel to the East and some Western countries require it as a routine for immigrants and visitors All members of H M Forces are vaccinated on entry unless genuine conscientious objection is raised

In Britain to-day vaccination for the civilian population is voluntary Long years of freedom have resulted in public apathy so that at present not more than 35 per cent of the child population has been vaccinated This is a matter for concern and means that smallpox epidemics are once more a distinct possibility Every doctor should urge his patients to have their children vaccinated Com munity interests apart from an individual s point

of view the routine practice of infant vaccination has much to recommend it The only serious com plication of vaccination is the rare vaccinia encephalitis This is almost unknown after primary *infant* vaccination and does not occur after re vaccination nearly all the recorded cases have fol lowed *primary vaccination of an adult* Nowadays more and more people travel abroad on civil or military business and they needs must be vaccinated if they intend to visit or pass through endemic smallpox areas Those previously unvaccinated will be exposed to a risk albeit a small one of vaccinia encephalitis a risk which would have been avoided if they had been vaccinated in infancy

Technique For primary inoculation the site usually chosen is the skin over the insertion of the deltoid but the thigh or abdomen may be used if it is thought desirable to have a less conspicuous resultant scar After preliminary skin cleansing a drop of calf lymph is placed on the site and then with an ordinary sewing needle held flat against *the skin some 12–24 pressures are made through* the drop The point of the needle should not pene trate but merely indent the skin and the pressures are spread over a small area about 0 5 cm in diameter This is the multiple pressure technique of vaccination and is preferred by most vaccinators For re vaccination about 20–30 pressures are desirable

An alternative method is to make a small single scratch through the drop of lymph This is more likely to ensure a successful take but increases the chance of accidental secondary infection and of subsequent scarring

Clinical Picture After primary vaccination a small papule appears at the site of inoculation on *the fourth day After two further days it becomes* vesicular and pustular a few days later The pustule ruptures and a scab forms this eventually separates leaving a scar which after a multiple pressure vac cination is very small During the stages of vesicu lation and pustulation there is usually a moderate amount of inflammation *in the surrounding skin* enlargement and tenderness of the associated lymph glands and often some pyrexia and general malaise

After re vaccination a similar but milder reaction *occurs the whole process being accelerated* The papule for example appears on the third day Constitutional disturbance is usually very slight. Individuals who have been re vaccinated many times may show very little response a small itchy papule may be the only sign of successful vacci nation

Failure of the vaccination to take may be due to poor technique or to out of date calf lymph The inoculation should be repeated using another site several times if necessary

Vaccination of *unprotected persons* who have been in contact with smallpox should if possible be carried out within 7 days of the exposure The disease will then almost certainly be prevented Vac *cination within 7–10 days of exposure will probably* make the attack mild but after that it is useless gamma globulin from recently vaccinated persons may however have some preventive effect

Complications Secondary infection of the inocu lation site is usually the result of carelessness

Generalized vaccinial pustulation is very rare but is more likely to occur in children with a tendency to eczema The resulting rash is similar to that of chicken pox

Vaccinia encephalitis is also rare and practically never occurs in small infants or after re vaccination It is however a serious complication with a mortality of about 35 per cent The onset is usually about 10 days after the primary vaccination

There *is* no *specific* treatment for generalized vaccinia or for encephalitis but gamma globulin from recently vaccinated individuals may help in some cases

Rickettsial Diseases

Q Fever

Q fever which results *from infection with Rickettsia burneti* was first identified in Australia but has since been found in many parts of the world It is not uncommon in Britain and as it is primarily a disease of cattle sheep and goats is more prevalent in rural areas The mode of trans mission from animal to man is not yet fully estab lished but in all probability the organism can be inhaled with farmyard dust and also ingested in milk or food contaminated by infected hands

Clinical Picture The incubation period is thought to be about 14 days The onset is usually abrupt with fever malaise and generalized aching Head ache is often severe and neck stiffness may be present In about half the cases described in Britain there have also been respiratory manifestations cough pleuritic pain and sometimes signs of wide spread bronchopneumonia or of lobar consolida tion Diarrhoea is an occasional feature and transient jaundice has been described

Course and Complications Though a patient with *Q fever can be quite ill with it complete spon* taneous recovery is the rule The acute illness lasts about a week and convalescence is usually rapid There are no complications

Diagnosis Unless the disease is known to be prevalent in a particular area clinical diagnosis can be only tentative for there are no characteristic features which distinguish Q fever from several other acute infections It is likely in fact that not a few attacks of the disease have in the past been thought to be influenza virus pneumonia and the like The white blood-cell count is unhelpful but there is a specific complement fixation blood test which can be carried out in specially-equipped laboratories A single titre of more than 1 40 is strong evidence and a rising titre is diagnostic

Treatment Chloramphenicol and the tetracyclines in 250 mg oral doses every 6 hr usually produce rapid improvement Many mild cases however require no more than rest in bed and aspirin

Typhus Fever

Typhus fever comprises epidemic or louse borne typhus and endemic or flea borne murine typhus The former a purely human disease caused by *Rickettsia prowazeki* is one of the classical plagues of mankind having for centuries followed in the wake of war and famine The mass movement of refugees and the crowding together of many starved dirty and lousy people creates ideal conditions for the spread of epidemic typhus because the organism is conveyed from one person to another by the common body louse (*Pediculus humanus*) and enters through its bites Epidemic typhus killed many victims in the concentration camps of World War II

Endemic typhus is a clinically similar but milder disease which is common in rat infested localities The causal organism is *Rickettsia mooseri* which infects the rats and is then carried to man by the rat flea (*Xenopsylla cheopsis*)

Typhus fever is still common in many parts of the world particularly the Far East, but has been extinct in Britain for many years

Clinical Picture The incubation period is about 14 days. The illness begins suddenly with high fever shivering and severe headache There is often a characteristic marked conjunctival injection Sore throat cough abdominal pains and neck stiffness are other common symptoms and mental confusion with convulsions often occurs Insomnia is the rule

About the fifth day of illness a characteristic skin rash appears This consists of reddish macules which often become petechial and appear first on the side of the trunk and insides of the arms Later the rash spreads to other parts of the body but avoids the face and neck.

Course and Complications. The patient s condition deteriorates with the onset of the rash He becomes extremely prostrated stuporose or delirious and without treatment often dies Cases which recover spontaneously do so quite suddenly about the end of the second week

As might be expected with such a severe prostrating illness numerous complications have been described They include bronchopneumonia myocarditis parotitis phlebothrombosis and peripheral neuritis Uncomplicated typhus however either kills or clears up without leaving any permanent sequelae

Diagnosis. During an epidemic this is straightforward but sporadic cases may not be identified till the characteristic rash appears In Britain the disease should be borne in mind when dealing with people recently arrived from the East, or with dockside dwellers

Complement fixation and agglutination tests on the blood are specific In addition the Weil Felix reaction is positive This is a blood test which depends on the fact that all rickettsia except those which cause Q fever and rickettsial pox produced in patients antibodies which agglutinate various strains of *Proteus vulgaris* In epidemic and endemic typhus the strains known as OX 19 and OX 2 are agglutinated single titres of more than 1 200 are diagnostic Lower titres may be obtained in the early stages of the illness but repeated tests will show a steady rise The tendency nowadays however is to replace the classical Weil Felix reaction with the more specific rickettsial antigen tests mentioned above

Treatment. Chloramphenicol and the tetracyclines are effective and 250 or 500 mg by mouth every 6 hr will produce rapid improvement. General treatment is a matter of maintaining an adequate fluid intake of sedating delirious patients and of careful nursing to avoid bed sores and parotitis

Prevention. This depends on cleanliness and the destruction of lice and fleas For the latter purpose 10 per cent dicophanum (D D T) powder is effective or a 2 per cent solution can be used to impregnate clothing Gammabenzene hexachloride (Gammexane) 1 per cent is even more lethal to lice These compounds however do not kill rickettsia so careful heat sterilization of bedding and other fomites is required in an actual case of typhus The attendants should wear special louse proof protective clothing

Scrub Typhus

Scrub typhus which is also known as mite borne typhus and as Tsutsugamushi disease is prevalent in the Far East and Pacific islands The causal organism is *Rickettsia orientalis* which infects rats and voles and is conveyed from them to man by a mite (*Trombicula*)

Clinical Picture The incubation period is from 7 to 21 days A small papule appears at the site of the mite bite which is usually on the ankle or lower leg and then breaks down to form a small shallow ulcer *At the same time there is fever with* chills and headache The local lymph glands become enlarged and tender and later a generalized adenomegaly may develop A macular skin rash similar to that of typhus fever may appear on the fifth day of illness not infrequently however it is absent

Course and Complications During the first week of illness the mind is clear but stupor and mental confusion tend to appear later A mild case will recover in a few days a severe attack may persist for a month The death rate is very variable and largely depends on the patient s previous state of health and nutrition The most important complica tion is an acute myocarditis leading to heart failure

Diagnosis This can often be made before the rash appears by noticing the primary bite lesion and observing the generalized glandular enlarge ment The Weil Felix reaction using the OXK strain of *Proteus vulgaris* is positive There are also available specific complement fixation and agglutin ation blood tests

Treatment This is the same as for typhus fever Dibutyl phthalate rubbed into the clothing is an effective *mite repellent*

Leptospiral and Treponemal Diseases

Leptospirosis Icterohaemorrhagica

This disorder which is also known as Weil s dis ease *results from infection with Leptospira ictero haemorrhagica* an organism which normally lives in rats It is usually acquired by contact with water or soil that has been contaminated by infected rat urine The leptospira penetrates through small skin abrasions Men are predominantly affected and farmers miners sewer workers and fish handlers *are most likely to acquire the disease Bathing in* rat infested rivers and streams can also result in infection

Weil s disease is probably a good deal more common in Britain than is generally recognized mild infections are often missed

Clinical Picture The incubation period is from *7 to 14 days The onset is sudden with high fever* headache muscular pains and vomiting There is often marked conjunctival injection Signs of lobar or of bronchopneumonia may appear and there may be a meningeal reaction with neck stiffness Albuminuria is often present

Many cases subside after a few days without *further manifestations but the more severe ones go* on to develop the jaundice and bleeding which give the disease its name Such symptoms appear about the fifth day and with their onset the tem perature begins to fall The jaundice is often deep and epistaxis haematemesis melaena and skin pur pura may occur

Course and Complications The death rate in Weil s disease is about 15 per cent but non icteric cases are seldom fatal When death occurs it is usually about the fourteenth day of the illness and is due to uraemia resulting from haemorrhagic nephritis In non fatal attacks recovery begins in the third week

Conjunctivitis pneumonia meningitis nephritis and haemorrhage are symptoms of the disease rather than complications They are seldom all pre sent in the same patient Iridocyclitis optic neuritis and endocarditis have also been described

Diagnosis Mild non icteric Weil s disease pre sents as a P U O and is often misdiagnosed as in fluenza The marked conjunctival injection that is usually present should raise suspicion however *especially if there is albuminuria* as well and should lead to inquiries about the possibility of contact with water in a rat infested neighbourhood When jaundice and haemorrhages are present diag nosis is easier but confusion with virus hepatitis may arise Virus hepatitis is not however accom panied by a leucocytosis in the blood whereas *Weil s disease is*

Leptospirae are present in the blood stream during the first week of illness If the blood is injected into a guinea pig subsequent examination of the pig s tissues will reveal the organism *Specific* agglutinins appear in the blood about the tenth day and a titre of at least 1 300 is diagnostic During convalescence leptospirae are excreted in the urine

Treatment There is no specific treatment for Weil s disease and antibiotics are of no value *Treatment should therefore be on the general lines* described on p 72 A high fluid intake is desirable to combat the possibility of uraemia

Patients should not be discharged from isolation till their urine is free from leptospirae as judged by direct dark ground microscopic examination and by guinea pig inoculation Nurses and laboratory *workers should handle such urine with circumspec* tion for the leptospira is a highly infective organ ism

Canicola Fever

About 20 cases of canicola fever are recognized annually in Britain but probably a number are missed The causal organism is *Leptospira canicola* which infects dogs Human disease usually arises after direct contact with infected dog urine but sometimes may result from bathing in contaminated water The organism penetrates through small skin abrasions

The symptoms of canicola fever are practically the same as those of Weil s disease but jaundice is uncommon and haemorrhage does not occur Death is rare

The diagnosis is made by demonstrating the organism in the blood and on the result of agglutination tests Treatment is on general lines as for Weil s disease

Syphilis

Syphilis which is also called lues or the pox is a chronic venereal infection caused by the *Treponema pallidum* (*Spirochaeta pallida*) and is usually acquired by genital inoculation during sexual intercourse It can also be transmitted during pregnancy by an infected mother to her unborn child in whom it produces the symptoms and signs of *congenital syphilis*

A disease which dates from antiquity syphilis has in the past been responsible for a great deal of sickness throughout the world In recent years however it has become relatively uncommon in civilized countries mainly because of much improved treatment and the increasing employment of effective prophylaxis

Acquired Syphilis The clinical course of acquired syphilis can be divided into three stages primary secondary and tertiary The three stages are not always clinically manifest however In one patient the primary and secondary symptoms may be transient and trivial and he may first become aware of the disease when the tertiary lesion appears In another tertiary lesions may never develop at all Moreover the progress of a syphilitic infection can be profoundly modified by treatment The following account of classical acquired syphilis should be read with these reservations in mind

Primary Stage In 9 cases out of 10 the primary inoculation lesion or hard chancre is on the genital organs in men it is usually on the prepuce or glans penis in women on the labia Extra genital chancres do occasionally occur on the lip or on the nipple as the result of kissing or at the anus as the result of pederasty

Th primary chancre first appears at any time between 10 and 90 days after the actual inoculation and is at first a red painless papule associated with marked induration of the surrounding tissue As a result of trauma and secondary infection the papule usually breaks down to form a small hard ulcer which bleeds easily At first the local lymph glands are painlessly enlarged but generalized adenomegaly follows during the second stage

The primary chancre heals in 2 to 8 weeks Unless secondary infection has been marked little or no permanent scarring remains

Secondary Stage 4 to 12 weeks after the appearance of the primary lesion signs and symptoms of generalized dissemination of infection appear though not infrequently they may be transient and slight A florid secondary stage however is marked by headache slight pyrexia vague generalized aching and a rash on both skin and mucous membranes

The skin rash is characteristically widespread symmetrical non irritating of a coppery colour and pleomorphic (*i e* different kinds of lesion are simultaneously present) The commonest lesion is a macule not unlike that of measles but papules appear on the forehead genitals and extremities and in moist situations like the axillae and perineum profuse and exuberant papular excrescences called condylomata may be present. Ulcerated nodular lesions are not uncommon and lesions like those of psoriasis or lichen planus are sometimes seen The hair often tends to fall out

On mucous membranes mucous patches which are superficial greyish painless areas of inflammation often develop especially on the lips inside the mouth and on the fauces Sometimes they break down to form characteristic slimy snail track ulcers Such lesions on the larynx may result in hoarseness

Hepatitis nephritis meningitis and splenic enlargement are occasional manifestations of the secondary stage

Tertiary Stage During the primary and secondary stages syphilis can be regarded as an acute infection Now however it dies down into a slow chronic disorder if indeed it persists at all Approximately 25 per cent of untreated syphilitics recover spontaneously after the primary or secondary stage Another 25 per cent do not completely recover in that their blood continues to give positive results on serological testing but the disease seems to remain permanently quiescent and the patient never develops any further clinical manifestations The remainder if untreated do after a latent period of 2 to 20 years slowly develop tertiary lesions but these may vary very much in severity The essential pathological process which occurs in the affected organs is a slow growth of syphilitic granulation

tissue associated with an obliterative endarteritis of the arterioles The granulation tissue forms a localized *gumma* which in superficial situations may break down to produce an ulcer with a char acteristic punched out appearance The endarter itis leads to tissue ischaemia and death with subse quent replacement by fibrous tissue

Any organ and tissue in the body can be attacked by syphilis in the tertiary stage though in com munities accustomed to the disease it is uncommon to find more than one or at the most two sites of assault in any particular patient However the pos sible clinical manifestations are numerous and are described in the various sections of this book that deal with system disorders

In Britain to day tertiary syphilitic disorders as a whole are relatively rare The once frequent ulcerating gummas of skin cartilage and bone are hardly ever seen while of the visceral lesions those affecting the cardio vascular and the central ner vous systems are predominant

Congenital Syphilis Recent syphilitic infection in a woman who becomes pregnant causes early abor tion If the disease remains active later pregnancies will usually last longer or may go to term though the child may be still born However eventually a live but congenitally syphilitic infant results and in time when the disease is chronic and only mildly active a normal child may appear This is the usual course of events but unexpected results sometimes occur For example a normal child may be followed by more congenitally infected offspring

The baby that has acquired syphilis *in utero* and which survives is often at first apparently normal Within a few weeks however it begins to show signs of widespread infection It fails to thrive and looks wrinkled and prematurely aged An early sign is the development of snuffles and a nasal discharge due to involvement of the naso pharynx In time the inflammation and destruction of the nasal cartilage produce the well known saddle nose deformity A variety of skin rashes appear about 2 months after birth Fissures (rhagades) develop at the corners of the mouth and mucous patches are often to be seen inside it The liver and spleen may enlarge and albuminuria is common Syphilitic epiphysitis causes painful joint swelling and consequent pseudo paralysis of the limbs while periostitis is visible when the long bones are X rayed

If the baby survives the hazards of intercurrent infection further symptoms appear during child hood and adolescence Mental and physical develop ment is often retarded Attacks of synovitis (Clutton s joints ') and of periostitis are common Interstitial keratitis leads to partial blindness and internal otitis to deafness The permanent teeth show characteristic deformities notched and peg shaped incisors (*Hutchinson s teeth*) and mul berry like (Moon s) molars During adolescence the symptoms of juvenile tabes and of general paralysis begin

Diagnosis In the primary and secondary stages of acquired syphilis and during the neo natal period of congenital syphilis the causal organism can often be identified Secretions from an ulcerated primary chancre from condylomata or from snail track ulcers or from the nasal or skin lesions of an infected infant when examined microscopically by a dark ground method reveal the presence of *Treponema pallidum*

In the tertiary stage of acquired disease and in congenitally syphilitic older children organisms are seldom recoverable and diagnosis depends on the demonstrations of antibodies in the blood or cerebro spinal fluid Serological tests of this kind include the Wassermann complement fixation re action and the Kahn and Meinicke flocculation tests The Wassermann reaction becomes positive in the blood about 3 weeks after the appearance of the primary chancre and in congenital disease is positive from birth It remains positive while in fection continues though isolated false negative results may sometimes be obtained It is also posi tive in yaws and leprosy diseases which have some resemblance to syphilis and may be temporarily positive during a variety of diseases e g vaccinia malaria glandular fever virus pneumonia trypano somiasis lupus erythematosus subacute bacterial endocarditis and typhus fever Repeated tests over a period of some months may therefore be neces sary to establish a firm diagnosis of chronic latent syphilis It must also be remembered that a repeatedly positive W R only means syphilitic *infection* and not necessarily syphilitic *disease* Patients with quiescent or with symptomless tertiary syphilis may acquire other disorders and it would be a grievous error to regard every manifestation of disease in them as necessarily of syphilitic origin merely because the W R is permanently positive

A positive W R in the cerebro spinal fluid of a syphilitic patient indicates that the disease has spread to the central nervous system even though no neurological symptoms or signs may be present False negative results are less common in the cerebro spinal fluid than in the blood so that in a suspected case of syphilis with an unexpectedly negative blood test it is a good plan to repeat the test on the cerebro spinal fluid Nevertheless a nega tive cerebro spinal fluid W R does not exclude syphilis but merely means that it has not yet in volved the central nervous system

From the above it will be seen that the interpretation of serological tests for syphilis is not always straightforward and that results must be examined carefully in the light of clinical findings In case of doubt, the tests must be repeated if necessary several times and in different laboratories for errors of laboratory technique can easily occur Syphilis has important social implications and considerable distress may be caused by a hasty diagnosis based on a single falsely positive blood test. It is equally foolish to allow legitimate clinical suspicions to be lulled by one false negative result

Treatment. For many years the treatment of syphilis consisted of prolonged course of arsenic bismuth and potassium iodide but penicillin has now almost replaced all these drugs The earlier treatment begins the better the result hence the importance of early diagnosis

For primary or secondary syphilis the total dosage of penicillin should normally be about 5 million units This is usually given in the form of daily intramuscular injections of 600 000 units of procaine penicillin for a period of 8 to 10 days Serious reactions to this treatment are rare but sometimes it may cause a temporary exacerbation of symptoms and even a sharp rise of temperature (Herxheimer reaction) Moderate reactions of this type do not call for any interruption of treatment

If penicillin is contra indicated because of known sensitivity one of the tetracycline group of antibiotics can be used instead

Whether there is any advantage in following the penicillin treatment with a routine course of arsenic and/or bismuth is at present uncertain With penicillin alone 90 per cent of early cases are cured the blood W R becoming persistently negative within 3 months of starting treatment Nevertheless careful follow up is necessary to detect the small percentage of cases that relapse or are resistant to treatment Such patients are treated with organic arsenical compounds like neoarsphenamine in 0 45–0 6 g intravenous doses weekly for 8 to 10 weeks When bismuth is employed the dosage is 0 2 g of bismuth metal intramuscularly every week for 8 weeks

Tertiary syphilitic lesions are in general treated along the same lines It is customary to start with oral potassium iodide which is a mild spirochaetocide in dosage increasing from 3–12 g (45–180 gr) daily After a week or two penicillin is added in similar dosage to that employed for primary lesions but repeated courses may be required to eradicate the disease

In cardiovascular syphilis it is particularly important to avoid Herxheimer reactions with consequent severe exacerbation of symptoms The initial penicillin dosage should be low (200 000 units daily) and the patient should be kept at rest under close supervision (*see* p 287)

In the treatment of neurosyphilis penicillin is often supplemented by malaria therapy (*see* p 407)

Congenital syphilis in infants is eminently curable but in older children is often resistant Babies should receive first an intramuscular test dose of 5 000 units of procaine penicillin and if no Herxheimer reaction follows 100 000 units are given daily for 10 days Alternatively the drug can be administered orally for a similar period in the 4 hourly bottle feeds the daily dosage being 50 000 units for each pound of body weight

The efficiency of treatment is judged by the disappearance of symptoms and signs and by the effect on the blood and cerebro spinal fluid Wassermann reactions Careful follow up is essential and no patient can be considered as cured until his serological reactions have been consistently negative for a period of 3 years after cessation of treatment. The blood W R should be tested every 3 months during the first year of this period and thereafter every 6 months The cerebro spinal fluid should be examined at least twice during the first year and thereafter if and when there is any suspicion of relapse

The symptomatic treatment of local syphilitic tertiary or congenital lesions is dealt with in the sections devoted to system diseases

Prevention. The use of a condom affords good protection against coital syphilis for both partners at least so far as the parts covered are concerned Careful washing after coitus has also some preventive effect as has the application of penicillin ointment Claims have been made for the efficacy of a single intramuscular dose of 2 400 000 units of benzathine penicillin (a long acting penicillin preparation) during the incubation period of the disease However there is always a danger that such prophylactic treatment may do no more than mask the disease by preventing the appearance of early symptoms and it is wise to follow it up with serological tests for not less than 3 months

For information on public health measures to check the spread of venereal disease textbooks of venereology should be consulted

DISEASES CAUSED BY HELMINTHS

Man can be the host to a large variety of worm parasites or helminths Most of them live in the alimentary tract and the majority do no great harm though their manifest presence often gives rise to anxiety and disgust Worm infestations are more common in tropical and subtropical countries particularly when the standards of sanitation and hygiene are poor Those which occur in Britain and which are of clinical importance will now be described

Tape-Worms (Cestodes)

There are four tape worms of clinical significance *Taenia saginata* the beef tape worm *Taenia solium* the pork tape worm *Taenia echinococcus* and *Diphyllobothrium latum* the fish tape warm Infestation by the first three occurs in Britain

The worms vary in size but each consists of a head or scolex to which is attached a string of flat segments or proglottides gradually increasing in size towards the tail From time to time one or more segments become detached from the tail but as new proglottides are constantly being formed at the head end the length of the worm does not diminish Each segment contains a uterus in which ova develop when mature they are discharged

Nearly all tape worms have two hosts The adult worm lives in the intestines of one host absorbing nourishment from the food therein and avoiding dislodgement by clinging to the mucous membrane by means of hooks or suckers on its head Its ova are discharged in the host s faeces and are then ingested by the second host in which they form larvae that are carried by the bloodstream to be deposited as larval cysts in the muscles and other organs When the second host is eaten by the first the larvae develop into adult worms

Man is the only host for the adult forms of *Taenia saginata* and *Taenia solium* The former which in Britain is the more common has its larval form in cattle while the latter prefers pigs Human infestation therefore results from eating infected beef or pork but proper cooking destroys the larvae and only those who go in for underdone meat are at risk Both worms when fully grown may attain a length of several yards

It is widely believed that tape worm infestation leads to loss of weight despite an increased appetite In fact the majority of tape worms produce no symptoms at all until the discovery of segments in the faeces reveals their presence After that auto suggestion will often produce a variety of symptoms

Diphyllobothrium latum a very long worm which may measure more than 50 ft has its larval form in fish and its adult form in dogs cats or human beings Infestation is met with mostly in fishing communities on the shores of the Baltic and in North America and does not occur in Britain The chief interest of this worm lies in its capacity to cause occasional macrocytic anaemia by interfering with absorption of the haemopoietic factor

Cysticercosis occurs in man when he ingests the ova of *Taenia solium* very rarely if ever when he swallows those of *Taenia saginata* The ingested ova may have come from another person or in the case of an individual with adult worm infestation from his own faeces Larval cysts or cysticerci are formed in the muscles and subcutaneous tissues where they usually cause no trouble but occasionally they may be deposited in the brain when they may give rise to epileptic attacks or in the eye where they cause inflammation

Hydatid disease is the result of infestation by *Echinococcus granulosus* (*Taenia echinococcus*) but in the case of this very small worm it is the larval form which affects man as well as sheep cattle and pigs the adult form occurs in the dog The disease is world wide and is not uncommon in Britain especially among country folk The ovum when swallowed penetrates the intestinal wall and enters the blood stream in which it is carried to the liver or less commonly to the lungs brain spleen or other organs there it develops into a larval hydatid cyst Such a cyst is filled with fluid and has an external laminated layer and an inner germinal layer which produces scolices and daughter cysts Gradual growth of the cyst takes place over the years and very large numbers of daughter cysts and grand daughter cysts may be formed within the original cyst The life-cycle of the worm is completed when the host dies and dogs devour its carcase

Hydatid disease in man is not often fatal As a rule only one organ is affected and only one or two cysts are formed Hepatic cysts produce no symptoms as a rule except gradual enlargement of the liver which may be observed by the patient himself or detected on routine examination Infection of the cyst may occasionally occur in which case the symptoms will be those of a liver abscess Spontaneous rupture into the peritoneal cavity is unusual but a serious matter when it happens for not only is there a severe general reaction with pyrexia but the result will be to disseminate daughter cysts throughout the abdomen Rupture through the diaphragm into the lung has occasionally occurred

Cysts of the lung are usually to be found in the right lower lobe and are often symptomless though cough and haemoptysis sometimes occur The cyst may rupture when its contents will appear in the sputum Secondary infection is not uncommon with consequent symptoms of a pulmonary abscess

Diagnosis Detection of adult tape worm infestation is a simple matter for examination of the stools will reveal the presence of cast off segments Very often the patient will have observed them for himself It is not important to establish which variety of taenia is present for the treatment is the same for all

Cysticercosis is rare in Britain but commoner in Eastern countries where *Taenia solium* abounds Diagnosis is by muscle biopsy or because after some years the cysticerci die and become calcified by X ray of the limb muscles and the diaphragm for which muscle the cysticerci have a predilection

Hydatid disease of the liver should be suspected when an individual who has to do with dogs develops symptomless hepatic enlargement and other causes of hepatomegaly have as far as possible been excluded Occasionally calcification in the wall of an old standing cyst may be detectable on X ray The Casoni test consists of the intradermal injection of 0 2 ml of hydatid fluid and a positive result indicating hydatid infection is shown by the development within 30 minutes of a large urticarial wheal at least 15 mm in diameter at the site of inoculation There is also a hydatid complement fixation test which can be performed on the blood serum but unfortunately false negative findings are common with both this test and the Casoni test Diagnostic liver puncture should be avoided in suspected hydatid disease for it carries a risk of rupturing the cyst or of producing subsequent leakage of its contents into the pleural or peritoneal spaces Sometimes a firm diagnosis of hydatid disease of the liver can be made only by laparotomy

Hydatid cysts of the lung appear as spherical shadows on X ray Those in the brain are nearly always diagnosed as cerebral tumours their true nature being revealed at operation

In all kinds of worm infestation there may be an eosinophilia in the blood its absence however by no means excludes such a diagnosis In hydatid disease for example only about 25 per cent of cases display eosinophilia though it is almost invariably present when any leakage of fluid from the cyst occurs

Treatment A patient with adult tape worm infestation should be kept on a very light diet for 2 days then on the morning of the third day given an oral dose of 4–6 ml (60–90 minims) of the Liquid Extract of Male Fern (Filix Mas) The drug is unpleasantly nauseating so is usually dispensed in capsules each containing 15 minims one of which is swallowed every 15 minutes Finally 3 or 4 teaspoonfuls of Epsom salts are given to ensure thorough bowel evacuation

If the scolex is not dislodged and passed as the result of this treatment the worm will re form later If desired the stools can be strained through black muslin in an attempt to identify the scolex However this is an unpleasant and laborious task and it is simpler to wait and see what happens If the worm re forms the same treatment can be given again a few weeks later or another drug can be tried Mepacrine 1 g has not proved to be outstandingly more successful than male fern extract but claims have recently been made for the efficiency of dichlorophen given in a dosage of 0 5 g for every 16 lb of body weight Other drugs such as hexylresorcinol or carbon tetrachloride are either more toxic or less effective worm killers

There is no curative treatment for cysticercosis Epileptic fits caused by the presence of cysticerci in the brain are treated on the same lines as idiopathic epilepsy (*see* p 461)

Hydatid cysts must be treated surgically being either removed entirely or if this is impossible marsupialized

Round worms (Nematodes)

Many round worms infest mankind Most of them live in the alimentary canal but some like Trichinella inhabit the muscles and connective tissues Round worms are non segmented circular in section taper at the ends and are of varying length

Oxyuris (*Enterobius vermicularis*) is also known as the thread worm and is a small whitish worm about 1 cm long which does look like a short piece of dirty cotton thread There are male and female thread worms which inhabit the colon but only the females survive the act of copulation after which they migrate down the alimentary canal to lay their eggs round the anus Intense anal itching results and as the sufferer is usually a child scratching follows The fingers then convey the eggs to the mouth and a vicious circle of re infection is set up

Oxyuris infestation is not in itself particularly harmful but loss of sleep due to irritation makes the child fretful and out of sorts and the scratching may lead to secondary infection of the perineum The disease is common in Britain especially among dirty children and adults

Ascaris lumbricoides is a large worm 15 to 25 cm in length which looks very like an ordinary earth

worm Ascariasis is common throughout the world human infection being usually acquired from mice rats rabbits or pigs which also act as hosts to the worm

Male and female worms live in the small intestine of their host and ova are passed in the faeces When the eggs are ingested they develop into larvae which then pursue a curious course After penetrating the intestinal mucosa they are carried in the blood stream to the lungs where they enter a bronchus travel up to the epiglottis and migrate down the oesophagus to reach the small intestine again where they develop into adult worms

Ascaris infestation causes few symptoms and is usually detected when worms are passed in the faeces or, less commonly are vomited up There may however be some general ill health and large collections of worms have been known to produce intestinal obstruction

The Hookworms (*Ancylostoma duodenale* and *Necator Americanus*) are capable of causing severe illness for they are blood suckers and produce a hypochromic anaemia They are very small worms about 0 75 cm in length which live in the duodenum and jejunum clinging to the mucous membrane by means of hook like teeth Ova are passed in the faeces and develop into larvae in damp soil or in water These larvae can penetrate the intact skin so infection is usually acquired by walking barefoot over contaminated ground or the larvae may be swallowed in infected drinking water

The entrance of larvae through the skin produces local irritation (ground itch) and a heavy in vasion may result in fever often associated with marked eosinophilia In the subcutaneous tissues the larvae enter a venule and are carried in the blood stream to the lungs There they enter the bronchi find their way up to the epiglottis and then migrate down the oesophagus to the duodenum

Ancylostomiasis causes anaemia asthenia and loss of weight if the infection remains unchecked death may eventually result The disease is most common in tropical and subtropical countries but has in the past occurred among Cornish tin miners and is sometimes reported from parts of the Euro pean continent

Trichinella spiralis is a small worm which nor mally inhabits the intestine of pigs Its larvae migrate into the pig s muscles where they form tiny cysts that remain dormant until the pig is eaten by man or by some other animal. Proper cooking destroys them so that trichinosis is only acquired when infected pork or sausage meat is eaten semi raw In the human intestine the ingested larval cysts develop into adult worms and may cause a mild temporary diarrhoea The adult worms in turn pro duce larvae which form cysts in the muscles and other organs This migration of larvae from the in testine to the muscles occurs about a week after eating the infected pork and is usually accom panied by fever urticaria oedema of the eyelids eosinophilia and muscular pains which may be severe Death is uncommon and recovery usually follows after 2 or 3 weeks but chronic muscular pains may persist for years After a long time the cysts die and become calcified

Trichinosis is a rare disease but small epidemics have occurred in Britain

Trichuris trichiuria the whip-worm is a tiny worm about 0 5 cm in length which lives in the intestine Its hind part is straight like the handle of a whip and the flexible forepart which is like the lash is embedded in the mucous membrane Ova are passed in the faeces

Trichuriasis is rare and is usually symptomless

Diagnosis Oxyuris and ascaris infestations are easily detected for the worms are to be seen in the stools from time to time Children with thread worms may not notice them however and often present simply as cases of persistent pruritus ani A quick method of diagnosis is to apply a piece of sticky transparent cellulose tape to the perianal region The thread worm ova will adhere to the tape and will be seen when it is examined under the microscope

Hook worm infection is proved by finding ova in the faeces and should be suspected when an individual who has lived abroad presents with hypochromic anaemia and eosinophilia

Trichinosis can only be diagnosed with certainty by muscle biopsy the biceps femoris deltoid or gastrocnemius muscles being most suitable for this purpose but any obscure febrile illness with muscle pains and urticaria should prompt enquiries as to the possibility of undercooked pork or sausage having been eaten and should warrant a blood count to detect eosinophilia In the chronic stage of the disease X rays of the muscle may reveal the presence of calcified dead cysts

Trichuriasis being a symptomless condition is usually discovered accidentally Microscopic exam ination of the stools reveals characteristic barrel shaped ova

Treatment Thread worms can be killed by p benzyphenyl carbamate (Diphenan) which is given by mouth three times daily for a week 0 125 g (2 gr) doses are suitable for a small child and 0 5 g (8 gr) for an adult If the infestation is not cleared by one course of treatment a second may be given after a week s interval or gentian violet pills 4–65 mg (1/16 to 1 gr) thrice daily for a week can be tried Piperazine hydrate 50–75 mg/kg

of body weight daily for a week is another effective remedy Ammoniated mercury ointment with 10 per cent benzocaine added to allay itching is applied to the anus in order to kill extruded worms and ova Re infection must be prevented by careful hand washing and by the wearing of plastic pants at night.

Hexylresorcinol is a fairly effective remedy for ascaris and hook worms as well as for thread worms 1 g (15 gr) is the dose for an adult and the drug is given orally in gelatin capsules and on an empty stomach It is followed 2 hr later by 2 or 3 teaspoonfuls of Epsom salts One dose of hexyl resorcinol will clear most ascaris infestations but two or three on successive days may be needed to cure ancylostomiasis Resistant cases may yield to a similar regime employing tetrachlorethylene 2–4 ml (30–60 minims) either alone or combined with oil of chenopodium 1–3 ml (15–45 minims) Tetra chlorethylene is however inclined to cause dizzi ness and patients to whom it is given should be in bed

Patients with ancylostomiasis will in addition require extra nourishment iron and blood trans fusion if their anaemia is severe

There is no treatment for trichinosis other than analgesics

Trichuriasis is difficult to eradicate but hexyl resorcinol should be tried if the patient wishes to have treatment

Flukes (Trematodes)

Flukes are small unsegmented parasites which may infest various human organs notably the liver lungs intestine and blood stream Fluke in festation is very rare in Britain but schistosomiasis may occasionally be seen in travellers who have returned from tropical areas where the disease is common

Schistosomiasis (Bilharziasis) is a chronic disease caused by one of three varieties of Schistosoma *S haematobium* which is found in Africa *S man soni* which is found in Africa and South America and *S japonicum* which is found in the Far East Urinary bladder symptoms tend to dominate the clinical picture of *S haematobium* infection whereas intestinal symptoms are more prominent with the other varieties

The fluke s second host is one of a variety of small water snails in which its ova develop into sporocysts which in turn produce numerous cercaria These cercaria leave the snail and swim about in the water hoping to find an unwary bather for unless they succeed in entering a suitable host within 24 hr they die They can either pierce the intact human skin or be ingested Once in the body they enter the blood stream and are carried to various organs the urinary bladder colon and rectum liver lungs and brain are most likely to be affected Ova are laid in the small venules that drain the organ and their presence causes consider able inflammation and ulceration Ova are dis charged in the urine faeces or sputum and when they get into water enter a snail.

The symptoms of schistosomiasis are those of a chronic cystitis colitis and proctitis occasionally complicated by hepatic cirrhosis chronic pneu monitis or encephalitis For detailed descriptions textbooks of tropical medicine should be con sulted.

Diagnosis This depends on discovery of the characteristic ova each equipped with a sharp spine in the dejecta from infected organs Schistoso miasis should be borne in mind when dealing with patients who have lived in Africa or the Far East

Treatment. Various antimony compounds are used For example tartar emetic (antimony and potassium tartrate) in 5 per cent glucose saline is given intravenously in 30–180 mg (½–2½ gr) doses daily up to a total amount of 1 5–2 g Miracil D (Nilodin) is a synthetic drug which can be given by mouth The dosage is 1 g twice daily for 3 days followed by a similar course a month later

CHAPTER 8

Tropical Infections

JOHN W TODD

THE infections which are common in the hotter parts of the world are usually described as the tropical diseases though the incidence of many is higher in many sub tropical countries than in the Tropics themselves and some (such as malaria) are endemic far into the temperate zones In this chapter only those tropical infections which may develop persist or recur after the subjects return to temperate countries will be considered since they may come into the differential diagnosis of obscure fevers alimentary upsets and other disorders Typhus is dealt with on p 95 along with the other rickettsial fevers and the worms on p 100

Perhaps the most striking feature of the tropical infections is their high incidence In many countries almost the entire native population is infested by hookworm and the majority by one or several other varieties of worm as well In addition most harbour malarial parasites and have enlarged spleens due to previous malarial attacks and many have the cysts of *Entamoeba histolytica* in their stools and carry various insects under or on their skin or in their hair They may also have non tropical infections such as syphilis gonorrhoea or tuberculosis in far higher incidence than is ever seen in Britain

These widely dispersed organisms are not always responsible for persistent symptoms and some such as certain of the worms are fairly harmless all the time In so far as they do cause symptoms these often occur in attacks with intervals of freedom (though some organisms are responsible for chronic ill health) Whereas in Britain only two common specific infections—tuberculosis and syphilis—are chronic or relapsing among the tropical infections malaria amoebiasis trypanosomiasis leishmaniasis leprosy and yaws are all more or less chronic and relapsing

Even in temperate countries the error of wrongly attributing to an infection an illness which in fact is coincidental is made occasionally A patient with a positive Wasserman reaction may develop a lesion which is wrongly thought to be syphilitic a patient with chronic pulmonary tuberculosis may develop a pulmonary infection due to another organism but wrongly attributed to tuberculosis In the Tropics the opportunities of making this sort of error are great and it cannot be emphasized too strongly that the discovery of a pathogenic organism does not prove that the patient s illness is necessarily due to this organism This error is not only made in the individual case in the past certain syndromes have been widely but wrongly attributed to a coincidental infection Kala azar was thought to be malarial because most of those with the disease were found to be harbouring malarial parasites This theory was discarded when it was found that a similarly high proportion of those free of kala azar in the same areas harboured malarial parasites The same mistake was made with hookworm which was also thought to be the cause of kala azar because nearly all those affected by it were found to harbour hookworms

In temperate countries it is a sound rule not to diagnose two independent acute diseases simultaneously In the Tropics no such rule can be made Even there the most common explanation of the presence of two or more pathogenic organisms is that one only is related to the current illness the others being at this time innocent Yet in many tropical regions acute infective illnesses are so common that two frequently develop more or less simultaneously and not rarely there may be three or four A familiar combination is malaria and acute bacillary dysentery If malaria only is recognized the wrong conclusion that the dysenteric symptoms are malarial is reached if only the dysentery is recognized the fever and sweats are wrongly thought to be dysenteric

Since the great majority of the tropical infections are alimentary or insect spread there are obvious means of preventing them If all water is boiled or otherwise sterilized if all food is eaten hot except when it can be peeled and if mosquito nets and insect repellents are used and only the minimum area of skin is exposed the chances of avoiding infection are greatly increased But although something can be done by such individual efforts the surest means of preventing insect borne infections is the destruction of the insects while alimentary spread infections can best be prevented by a main drainage

system piped clean water and constant care in handling food Such measures are extremely expensive

Many of the most important tropical infections are protozoal they include malaria trypanosomiasis amoebiasis and leishmaniasis By contrast protozoal infections very rarely arise in Britain Yaws another common tropical disease is due to a spirochaete Specific drugs for all these infections were discovered before the sulphonamides and antibiotics In 1930 the tropical physician could cure or greatly ameliorate all these conditions at the same time his colleague in Britain was virtually impotent before all infections except syphilis Even now there are few things in medicine more dramatic than the effect of quinine on malaria and few more remarkable than the improvement in the prognosis of kala azar by antimony In the past this disease was nearly always fatal now the victims of most forms of it nearly always recover

Malaria

Malaria is due to infection by various species of the protozoan *Plasmodium* which are transmitted by certain anopheline mosquitoes Although hookworm infestation has an even higher incidence malaria without doubt causes and from the dawn of history has caused more illness throughout the world than any other infection In most of the tropical and subtropical countries the vast majority of the indigenous peoples harbour the parasite at times and suffer varying amounts of ill health as the result The malarial death rate is difficult to assess but it is estimated that in India some 2 million people die from it annually The very high infant mortality can be largely attributed to this disease

Severe illness and death from malaria is chiefly due to *P falciparum* infection which is responsible for the malignant tertian variety of the disease and is largely limited to the hottest areas Benign tertian malaria is due to *P vivax* and is much less serious It is widespread not only in the tropics and subtropics but also in Southern Europe and other temperate countries and it occurs as far North as Holland and parts of Sweden and Russia It used to occur in Britain until the last century but in recent years the only fresh cases were seen after the two world wars no doubt as the result of the return of numerous ex servicemen harbouring the parasites which infected the local anopheline mosquitoes In turn these mosquitoes infected other people No fresh cases have been reported in Britain during the last few years so it is now safe to assume that an illness is not malarial unless the patient has previously lived in a malarious country or has been artificially infected for the purpose of treating dementia paralytica or other disease

Quartan malaria (due to *P malariae*) is very much less common than the other two varieties Ovale tertian malaria (due to *P ovale*) is extremely rare and found only in a few localities

Aetiology The infected female anopheline mosquito injects saliva into man containing the form of parasites known as *sporozoites* These circulate in the blood stream for some 2 hours and then become localized to the parenchymal cells of the liver where they grow and divide by schizogony into some 30 000 portions each of which develops into a *merozoite* These are later released into the blood stream as the result of the rupture of the distended liver cells Each *merozoite* may then invade a red blood corpuscle where it develops into the ring form and later divides by schizogony and is then known as a *schizont* The red blood corpuscle in time ruptures and the parasites invade other red corpuscles Several cycles of this asexual reproduction take place followed by the development of some parasites into the sexual form the male and female *gametocytes* Only the *gametocytes* can infect mosquitoes and in them there is a further cycle resulting in the development of the *sporozoites* which in turn infect man

The hepatic forms of *P falciparum* seem to be capable of invading red blood corpuscles only but the hepatic forms of *P vivax* *P malariae* and *P ovale* may sometimes invade other liver cells The parasites in these secondarily invaded liver cells may not mature for long periods and are probably responsible for distant relapses Such relapses due to *P falciparum* do not occur

Pathology The growth and multiplication of parasites in the red cells causes their rupture and the simultaneous liberation of the parasites and of the destroyed red cells into the circulation is responsible for the malarial paroxysms The released and altered haemoglobin is taken up by the reticulo endothelial cells in the spleen liver bone marrow and elsewhere There is marked formation of bile pigment urobilinogen and urobilin are increased in the urine and when the cell destruction is great jaundice develops There is always some degree of haemolytic anaemia which is very marked when the infection is severe and untreated

The spleen becomes enlarged sometimes very rapidly At first it is soft but with repeated infections it may become hard and very large often with infarcts The liver also is enlarged When the red cells are infected by *P falciparum* they may adhere to each other and to the small blood vessel walls causing them to become blocked and emboli may follow If the brain is affected by this process

there may be haemorrhages causing the manifestations of cerebral malaria Affection of the stomach may cause haematemeses or of the lower bowel dysenteric symptoms

Clinical Picture In initial infections the malarial attack begins with such non specific manifestations as malaise headache and backache anorexia and fever The fever is often continuous for a few days especially when the infection is due to *P falciparum* Later the fever usually becomes periodic attacks occurring every 48 hr with *P vivax* (benign tertian) *P ovale* or *P falciparum* (malignant tertian) or every 72 hr with *P malariae* (quartan) Fever due to *P falciparum* however may be continuous or irregularly remittent for considerable periods or indefinitely

Each malarial paroxysm begins with a chill the patient having a sensation of intense cold (though the temperature at the time is rising) with shivering This phase lasts about an hour The hot stage follows in which there is a sensation of great heat with a hot dry skin headache and often vomiting The temperature may reach 102 –106 F or occasionally higher This phase lasts some 3 hr Finally the sweating stage suddenly develops with rapid fall of temperature most profuse sweating and the quick disappearance of headache and other associated symptoms The patient often feels quite well again very soon or merely exhausted and sleepy This phase also lasts about 3 hr

When the infection is due to *P falciparum* there may be no such clear cut paroxysms and the patient s condition may rapidly become very grave with profound toxaemia severe anaemia jaundice vomiting and diarrhoea Particularly when there is cerebral involvement death may soon occur preceded by convulsions mania or coma

If no treatment is given and the patient escapes death he acquires some immunity and the paroxysms become less intense and in time cease though relapses may occur irregularly for a few years These repeated attacks cause more or less severe chronic ill health with loss of weight weakness anaemia splenomegaly (which may be extreme) hepatomegaly and other symptoms

Acquired immunity seems to be specific for the particular strain of the particular species of *Plasmodium* When there are several strains of a species in a locality the development of immunity against them all may take a very long time Those who are immune to malaria in one place may again develop the disease when they move to another place where there are different strains or species

Effective treatment eradicates *P falciparum* infections completely though re infection may always occur *P vivax* and *P malariae* infections are not always eradicated by any scheme of treatment and people who have acquired these infections abroad and return to Britain may continue to have occasional relapses for years It is usually stated that *P vivax* relapses never continue for more than 3 or 4 years and *P malariae* relapses for more than 20 years But these statements depend on the observation that no one has succeeded in discovering the parasites after longer periods Those who have had *vivax* malaria commonly claim that their attacks persist for far longer than 4 years people are seen who acquired malaria in Salonika in 1917 and still have fever which they attribute to malaria The true explanation of their fever may well be some other infection but it should not be assumed that this popular belief must be false the malarial parasite may possibly change its habits over the years and continue to cause fever as the result of a process in the internal organs without appearing in the peripheral blood

Diagnosis It is often said that the only sound means of diagnosing malaria is the identification of the parasite But the problem is not nearly so simple as this for the following reasons

1 A few parasites can often be found in the blood of those who have developed immunity from repeated attacks even when they are well The wrong deduction can easily be made therefore that an illness in such a subject is malarial when in fact it is due to something else the malarial parasites being coincidental The discovery of parasites in the blood of the patient who has never previously had malaria or the discovery of a heavy infection in the subject who has had repeated attacks no doubt provides virtual proof that malarial illness is present but it does not prove that some other illness may not be present as well In the Tropics double infections are common

2 During the first stages of an initial malarial illness the parasites are not always discovered in the peripheral blood It is no answer to state even if it be true that if an expert parasitologist spends a very long time carefully studying a large number of blood slides he will always find a few parasites Such experts with sufficient time are not always available

3 The clinical picture of the typical malarial illness (with the chill the hot stage in which the temperature reaches a very high level and the sweating stage ending in a normal temperature occurring every 48 or 72 hr) is so characteristic as to make the clinical diagnosis as near a certainty as anything in medicine Moreover this picture virtually proves which the microscope can never do that the patient has no second infection causing fever in addition to malaria On the other hand

the absence of this typical illness does not exclude malaria particularly when the infecting organism is the *P falciparum*

Although then the discovery of malarial parasites is a valuable piece of information the diagnosis should be reached from a consideration of all available data The emphasis on the microscopic aspects of the problem becomes particularly absurd to the solitary doctor in a malarious country dealing with vast numbers of sick people and with only the sketchiest equipment it is he not the consultant physician with a large laboratory at his disposal who takes the lion s share of the fight against malaria

In malaria there is as a rule little risk that one of the cardinal principles of diagnosis—namely that a diagnosis is not made if the possibility of a condition is never considered—will be overlooked No doctor in a malarious country can fail to consider the possibility of the disease and the patient in a non malarious country who is subject to benign tertian relapses is apt to inform his doctor if he develops fever that he is sure he has malaria In these circumstances there is too great rather than too little a tendency to diagnose malaria But when someone in a non malarious country develops the disease for the first time neither he nor his doctor may think of it This may happen when suppressive drugs have been taken continuously during and after a previous stay in a malarious country but were later stopped or when someone has recently arrived from a malarious country especially if he has travelled by air Such cases are by no means rare When therefore a patient develops fever for which there is no obvious cause he should always be asked whether he has been abroad and has taken suppressive drugs In particular when someone who has recently arrived by air from a malarious country develops cerebral symptoms malignant tertian malaria should be the first diagnosis to be considered

The means of discovering the parasites is by the examination of blood films stained by one of the Romanowsky stains Thick and thin films of blood are taken the parasites can be seen more clearly and identified more easily on a thin film but if they are very scanty may be discovered only in a thick film The expert usually has little difficulty in recognizing the species of the parasites (though the patient may be infected by more than one species)

Prevention The complete destruction of anopheline mosquitoes is the only sure means of preventing the spread of the parasites Individual efforts to prevent mosquitoes from biting (by the use of nets and by covering most of the skin after dusk by clothing and smearing the remainder with repellent) are not completely effective and are a nuisance to carry out The only effective individual prophylactic is the continuous use of anti malarial drugs which suppress the clinical manifestations though they do not prevent the infection Proguanil (Paludrine) in doses of 100 mg daily and pyrimethamine (Daraprim) in doses of 25 mg weekly for an adult are probably the best They should be taken throughout the stay in a malarious area and for at least 2 weeks after leaving it They completely eradicate *P falciparum* (so that relapses due to this organism do not occur after the drugs have been stopped) and they prevent fever due to *P vivax P malariae* and *P ovale* though relapses due to these organisms are common when the drugs are no longer taken Other effective suppressive drugs are mepacrine in doses of 100 mg daily (though this has the disadvantage of staining the skin yellow) and chloroquine in doses of 300 mg weekly Quinine is less effective as a prophylactic than the drugs mentioned and may precipitate blackwater fever when subjects are exposed to *P falciparum* infection

Treatment The widely held dictum that treatment should not be given until the diagnosis has been established is not applicable to malaria especially when the patient is possibly infected by *P falciparum* It has already been pointed out that the discovery of the parasite does not prove that malarial illness is present and the failure to discover the parasite does not prove that malarial illness is absent Moreover there may be no facilities to examine the blood Although blood films should be taken and studied immediately if possible or otherwise later if there is the smallest suspicion of malignant tertian malaria an anti malarial drug should be given without delay Giving the drug unnecessarily can hardly do harm the failure to give it may kill the patient There is no such urgency when the point at issue is whether or not someone has benign tertian malaria but even here something is gained by immediate administration of a drug if malaria is present and nothing is lost if it is not Moreover in malarious countries the best way of preventing attacks is the continuous use of suppressive drugs which are taken by nearly all Europeans and by many of those natives who can afford them If therefore someone who has not been taking a drug continuously develops a febrile illness and then has some large preliminary doses followed by the usual suppressive course he is merely being placed in the same situation as his more sensible or fortunate fellows The failure of fever to respond to an anti malarial drug is a most valuable diagnostic indication by providing virtual proof that some other cause than malaria must be sought for the fever

The one situation in which anti malarial drugs may rightly be withheld until the parasites have been found is that of a patient in a non malarious country who develops a fever which may be a benign tertian relapse The knowledge that he is liable to such relapses is useful to him appreciable harm can hardly result from delay and if no parasites are found by an expert the disease is unlikely to be present

Treatment of Acute Attack A specific remedy for malaria in the shape of cinchona bark (whose essential principle is quinine) was probably used in South America for centuries before the European invasion Traditionally it was first introduced into Europe in 1638 by the Countess of Chinchon wife of the Viceroy of Peru though this story has recently been exploded The fame of the bark rapidly spread throughout the world However in India its use largely ceased in the nineteenth century because it was thought to be worthless and patients were instead treated by purging and blood letting Its failure can no doubt be attributed to the confusion between malaria and other causes of fever and to the use of bark containing only a small amount of quinine The only other specific drug which has been known for centuries is ipecacuanha (whose active principle is emetine) in the treatment of dysentery Apart from some vermifuges the next specific drug was mercury for syphilis which is not highly effective Only in this century have anti bacterial drugs comparable in efficacy with quinine been discovered

Even now quinine is probably just as effective in relieving an acute attack as are the modern synthetic drugs it should be given in doses of some 650 mg (10 gr) thrice daily for about a week Other drugs which may be used are mepacrine 300 mg thrice daily on the first day 200 mg thrice daily on the second day and 100 mg thrice daily for another 5 or so days proguanil (Paludrine) 100 mg thrice daily for about a week and chloroquine 900 mg on the first day and 600 mg for the next 2 or 3 days

When the patient is vomiting or has cerebral malaria the drugs should be given parenterally Intravenous quinine bihydrochloride given very slowly in a dose of about 1 g (15 gr) repeated after 8 hr or replaced by oral administration is highly effective Alternatively chloroquine sulphate 200 mg intravenously or mepacrine methane sulphonate 300 mg intramuscularly may be given followed by further similar amounts in about 8 hr or by the drugs by mouth

All other treatment is of trivial importance There is no good reason to keep the patient in bed after he has recovered from an acute attack Diet can be left to the patient s inclinations Anaemia due solely to malaria clears up when the infection is eradicated (though anaemia in the Tropics often has several causes)

Prevention of Relapses No known drug or combination of drugs will consistently eradicate *P vivax* or *P malariae* In a malarious area there is usually no need to take special measures to prevent relapses since the drugs which are being taken regularly to suppress new infections will also prevent the old ones from relapsing The problem chiefly arises therefore in non malarious areas The most effective way of dealing with it is to continue taking a regular drug such as proguanil 100 mg twice a week for the next few years A course of pamaquin 10 mg thrice daily for 5 days is said to lessen the chances of relapses thereafter but since this drug may cause serious toxic effects and is not consistently effective its use is unjustified Many people deal with the problem by waiting for a relapse to occur and they then immediately take a course of drugs such as was described for the treatment of the acute attack In view of the high efficiency of the drugs there is little objection to this policy

Blackwater Fever

This is a grave complication of *P falciparum* infections with a mortality of about 20 per cent It particularly occurs when inadequate and irregular quantities of quinine are being taken as a suppressive though the reason for its development is unknown Suddenly and accompanied by no evidence of a malarial relapse there is intravascular haemolysis of red cells This may last a few minutes or some hours may be an isolated event or recur at intervals for a few days and may involve a large or small proportion of the red cells After the process starts it is usually impossible to find parasites in the blood In severe cases intense jaundice and grave anaemia may develop within a few days Much of the liberated haemoglobin is excreted in the urine as oxy haemoglobin or methaemoglobin The urine is consequently dark hence the name of the syndrome Oliguria or anuria may occur This used to be attributed to the deposition of blood pigment in the collecting tubules causing mechanical blockage but it now seems that the renal failure is of the same nature as that accompanying various states of shock such as the crush syndrome and is related to the diminution of blood volume and blood pressure and peripheral circulatory failure

Blackwater fever is the one syndrome due to malaria of which the treatment is unsatisfactory The drugs which are so dramatically effective in other circumstances may even make matters worse by aggravating the haemolysis and this is thought to be particularly true of quinine It is probably

best to give no drugs at the onset but when recovery from the blackwater fever has occurred chloroquine proguanil or mepacrine should be given If adequate administration of one of these drugs is maintained thereafter further blackwater fever (and of course other malarial manifestations) will not occur

Recent observations have suggested that steroid drugs may have a most favourable effect on the course of blackwater fever in common with other varieties of acquired haemolytic anaemia (*see* p 491) But most of the other remedies for blackwater fever are of doubtful efficacy and it has been said that if the patient is left alone he will do better than if enthusiastically treated In particular giving massive quantities of intravenous fluid to the anuric subject in the hope of forcing the kidneys to work again and giving large amounts of alkali (both of which were until recently standard practice) in high probability lessened the chances of recovery Rather should the anuric subject be given the minimum amount of fluid needed to replace that lost in the sweat and breath The value of blood transfusion—which in view of the grave anaemia seems reasonable—is also most doubtful since the donors cells may be haemolysed

Amoebiasis

This is an infection of the large intestine and sometimes of the liver and even of the lung or other organs by the *Fntamoeba histolytica*

The organism may be found in the intestinal contents throughout the world but is most common in the hot regions where it can probably be isolated from some 20–50 per cent of the population Among people who have always lived in temperate zones symptoms due to amoebiasis are very rare but the cystic forms of the organism are thought to be common It has been said that the infection is present in 20 per cent of the inhabitants of the Southern United States and 5 per cent of the inhabitants of Britain and the Northern United States but widely different figures of the incidence of cysts have been given by different observers This is no doubt at least partly due to the difficulty of identifying cysts—a matter which is discussed further below Although the symptoms of amoebiasis rarely arise in the temperate zones people who have acquired the infection in the Tropics may continue to have recurrent attacks for some years after they return to temperate countries

Aetiology The infective form of *E histolytica* is the cyst which is passed in the stools of infected people and can survive for several days at least in *moist* surroundings The cysts may be present in vegetables which have been grown in contaminated ground or in food which has been handled by carriers whose fingers are contaminated with faeces The swallowed cysts may or may not develop into amoebae in the large intestine The factors which encourage this development are unknown though it is clear that they are commonly found in hot countries but rarely found in temperate countries The amoebae multiply by simple fission Later cysts may again develop which are passed in the faeces

Pathology The amoebae invade the mucosa and submucosa of the large intestine and multiply Areas of colliquative necrosis develop due to a ferment produced by the parasites The resultant small abscesses are bacteriologically sterile and there is no inflammatory reaction in the surrounding tissues The abscesses may spread and rupture into the bowel and the ulcers which develop become secondarily invaded by bacteria with a consequent inflammatory response The extent and severity of the process varies widely and repair of the lesions may occur at any stage as the result of the body s defence mechanisms (or of treatment) Later there may be a reactivation of the process

When the process is severe it may extend beyond the bowel wall to the surrounding structures secondary infection may occur and amoebomas which are inflammatory granulomatous tumours may develop Occasionally there is perforation of the bowel with resultant peritonitis Amoebae may invade the portal vein radicals and be carried to the liver where amoebic abscesses develop These consist of a colony of parasites in the periphery and lysed liver tissue which is bacteriologically sterile in the middle The abscesses may be scattered throughout the liver or be confined to one region and they may fuse to form large necrotic areas containing up to several pints of pus When near the diaphragm they may cause a pleural effusion or they may penetrate to the lung with resultant amoebic abscesses there The abdominal wall may also be penetrated Rarely embolic spread occurs to other organs

Clinical Picture Amoebic infection frequently causes no symptoms When symptoms occur they vary infinitely in severity and a characteristic feature of the disease is the exacerbations and remissions The interval between infection and the first symptoms probably varies between a few weeks and some years though in the individual case it is usually quite impossible to determine this interval (and in endemic areas re infection presumably occurs very often)

Typically the onset of alimentary amoebiasis is insidious with mild diarrhoea abdominal discomfort malaise and often some anorexia and loss of

weight These symptoms may subside in a few days and recur after some weeks When the process is more severe very numerous loose motions containing much blood and mucus are passed and the patient may become severely ill with profound weakness and rapid loss of weight In mild cases examination of the abdomen may reveal nothing beyond vague tenderness but in more severe and chronic cases a tender palpable ascending or descending colon may be felt

Amoebic hepatitis may at first cause only such general symptoms as malaise low irregular fever and loss of weight The initial local symptom is usually discomfort in the region of the liver There may later be severe pain and tenderness over or below the lower ribs with hepatic enlargement or if the pleura or lung are involved the manifestations of pleural effusion or cough with anchovy sauce sputum

Diagnosis It is often said just as with malaria that the only sound means of diagnosis is the identification of the parasites But here also the situation is not nearly so simple The discovery of vegetative forms of *E histolytica* is sufficient proof that active alimentary amoebiasis is present and the important practical questions are (1) What is the significance of cysts? and (2) Does the failure to find *the parasite exclude the disease?*

The first problem in regard to cysts in their correct identification This can be very difficult and mistakes are said to be made even by trained pathologists unless they have had special experience (and consequently it is suggested that suspect cases should if practicable be studied in special centres) An illustration of the difficulty is provided by the remarkable variations in the estimates of the cyst carriers in Britain

If it is accepted that cysts are those of *E histolytica* it may well be that the particular strain is non pathogenic The strains with large cysts are often said to be pathogenic whereas those with small cysts are said to be non pathogenic On the other hand it has been hypothesized that all strains can become pathogenic when placed in circumstances suitable for their development All strains are said to be pathogenic to experimental animals but even if this is true it does not prove that they are necessarily pathogenic to man There is then insufficient evidence to reach firm conclusions about this matter Even if cysts are in fact those of a pathogenic strain this does not prove that the patient s symptoms are due to amoebiasis The statement that up to 50 per cent of the inhabitants of endemic areas harbour the parasite if true supports this view

The difficulties of deciding the significance of what are thought to be *E histolytica* cysts are then so great that the only sound solution is to ignore them and reach the diagnosis by other means

Vegetative *E histolytica* are not always easily found in the stools of people with the milder and more insidious forms of alimentary amoebiasis and sometimes they are discovered only after days or weeks of searching Various means for improving the chances of discovery are advocated such as taking the bedpans direct to the laboratory after the stool has been passed taking swabs from ulcers seen through the sigmoidoscope and giving the patient doses of salts before his stools are examined. Since it can be so difficult to discover the organism it is reasonable to deduce that the failure to discover it cannot exclude amoebiasis

In the absence of vegetative *E histolytica* from the stools the decision as to whether or not a *patient has amoebiasis should therefore be made* on other than microscopic grounds In an endemic area or when a patient has recently returned there from the clinical picture of recurrent diarrhoea with malaise loss of weight a tender or palpable colon and perhaps anorexia and dyspeptic symptoms are sufficient grounds for giving anti amoebic drugs Sigmoidoscopy if it reveals ulcers with relatively normal mucous membrane between them is *also a suggestive finding (though normal sigmoidoscopic appearances cannot exclude the disease)*

The conditions likely to be confused with alimentary amoebiasis are bacillary dysentery non specific colitis and carcinoma Bacillary dysentery is usually an acute febrile self limited disease and the stools typically consist largely of blood and pus with little faecal material (though this is not always so) Microscopy shows numerous pus cells and the bacilli can usually be cultured But the presence of bacillary dysentery does not exclude amoebiasis in the Tropics they often occur together Non specific colitis is not accompanied by pathogenic organisms in the stools and through the sigmoidoscope generalized inflammation can be seen (whereas there are usually normal areas of mucous membrane between amoebic ulcers) In places where amoebiasis is common the diagnosis of non specific colitis should be made only with caution and in doubtful cases it is proper to do a therapeutic test by giving the anti amoebic drugs *On* the other hand in Britain non specific colitis *is far* commoner than amoebiasis and the latter diagnosis should be suspect unless there is a history of recurrent symptoms dating from a spell abroad and gravely suspect if the patient has never been abroad Carcinoma in the rectum and lower colon can be excluded as a cause of diarrhoea by the sigmoidoscope Colonic carcinoma out of reach of the sig

moidoscope is less likely to cause confusion and can often be detected by barium enema radiography But an amoeboma may closely simulate carcinoma clinically radiologically and by sigmoidoscope though scrapings may reveal amoebae When amoebiasis particularly affects the caecum it may suggest appendicitis and not rarely is accompanied by appendicitis by causing appendicular obstruction

In the diagnosis of amoebic hepatitis stool examination is unimportant since even the discovery of vegetative *E histolytica* cannot prove that the liver is involved and the absence of the organism means nothing This condition is apt to be overlooked unless the possibility of its presence is borne in mind particularly when it causes a pleural effusion or evidence of mischief at the right lung base since it is then easy to assume that a primary pleural or lung condition is present A valuable radiological sign is elevation and immobilization of the right half of the diaphragm Sterile pus can sometimes be aspirated from the enlarged tender liver It is questionable whether this is justifiable unless there appears to be a large amount of pus when aspiration should undoubtedly be performed (but as a therapeutic not a diagnostic measure) Moreover the failure to aspirate pus cannot prove that it is absent If there are good grounds for suspecting amoebic hepatitis a course of emetine may rightly be given and this is a most valuable therapeutic test since if this condition is present the response is usually dramatic

Prevention In endemic areas the parasite is widely dispersed throughout the alimentary tracts of the population and elsewhere and with present knowledge eradicating the organism is impracticable On theoretical grounds it can be argued that if food is boiled and eaten hot and if the stools of everyone in the kitchen are repeatedly examined to ensure that carriers are kept away the incidence of amoebiasis should fall But there is no proof that this result follows A possible means of prevention is the prolonged use of anti amoebic drugs This has not been employed on a large scale but there is good evidence that it is largely effective A suitable drug seems to be iodochlorhydroxyquin (Entero vioform) 0 25 g twice daily

Treatment Amoebiasis is a disease of infinitely varying severity whose natural course is of exacerbations and remissions The assessment of the long term value of remedies for diseases of this kind is most difficult and with amoebiasis there is the additional complication that relapses cannot be distinguished from re infections Conclusions about this matter which are not derived from large series of carefully studied cases with proper controls therefore should always be suspect Unfortunately these considerations have no more prevented confident statements being made about the treatment of amoebiasis than they have prevented similar confident statements about peptic ulcer or rheumatoid arthritis

Nevertheless the value of emetine in the acute phases of the disease seems certain for after it is given there is often an immediate and dramatic amelioration of the symptoms This effect is seen most strikingly in amoebic hepatitis the very ill patient with a high swinging fever and an enlarged tender liver is often almost well again within a very few days In the acute phases of alimentary amoebiasis the improvement may be nearly as great especially among people who are having their first attack The usual dose of emetine is 65 mg (1 gr) daily intramuscularly for at least 3 or 4 days There seems to be no good evidence as to whether prolonging the course to some 10 or 12 days gives extra benefits but such prolongation may do good and is unlikely to do harm For amoebic hepatitis the prolonged course should probably be given in every case

Emetine alone does not always prevent relapses and together with or following it many drugs are often used usually in combination These include emetine bismuth iodine (E B I) 200 mg (3 gr) in enteric coated capsules nightly for up to 10 nights (it is given at night because it causes nausea which will be prevented by sleep and a sedative is often taken with it) iodo quinoline preparations such as di iodohydroxyquinoline (Diodoquin) 0 6 g thrice daily or iodochlorhydroxyquin (Entero vioform) 0 25–0 5 g thrice daily for some 21 days or chiniofon retention enemas (about 300 ml of a 2 per cent solution) daily or on alternate days for some 14–21 days arsenical preparations such as acetarsol (Stovarsol) or carbasone 260 mg (4 gr) thrice daily for about 2 weeks chloroquine 300 mg thrice daily for a day or two followed by 300 mg daily for some 3 weeks (this drug is highly concentrated in the liver and is particularly effective for amoebic hepatitis) various anti bacterial drugs The tetracyclines are directly amoebicidal but they and other drugs including penicillin and the sulphonamides (which have no direct effect on the amoebae) also seem to play a useful part by rendering the bacterial flora of the intestine unfavourable for amoebae

A combination of drugs such as a course of emetine followed by E B I and Diodoquin and perhaps also an anti bacterial drug is probably more effective in clearing up an acute attack and less likely to be followed by relapse than is emetine alone But relapses may still occur though if the patient is removed to a country where the disease

is not endemic the relapses tend to become less frequent and less severe and in time the symptoms disappear altogether A possible though little used method of preventing relapses is by continuing to give one of the iodoquinoline drugs indefinitely (as described under Prevention)

Emphasis is often placed on the test of cure by examining the stools repeatedly—say for 12 consecutive days after the treatment is finished and again at intervals for months But the best test of cure is the disappearance of symptoms The difficulties of interpreting cysts have already been considered and even the right conclusion that *E histolytica* cysts are present provides no evidence that the patient will later have a relapse

Treatment other than by drugs is unimportant Rest in bed is often advised during the acute phase If the patient has severe symptoms this is reasonable but there is no evidence that the course of the disease is altered by the rest Rest is also advised because emetine is said to have a toxic effect on the heart but even if this is so it is not apparent why remaining in bed should be beneficial A residue free diet is often given on theoretical grounds but as there is no evidence that it does good diet may be left to the patient s inclinations

Kala azar (Visceral Leishmaniasis)

This is an infection by the protozoon *Leishmania donovani* It is transmitted to man by biting sand flies of the genus *Phlebotomus* in the intestines of which the parasites multiply after infected blood has been sucked Flagellated forms of the parasite later appear in the insect s pharynx and pass into the blood stream of man when next it bites

The disease occurs particularly in Assam and Bengal where epidemics are common also in other parts of India on the Mediterranean seaboard the Sudan Kenya and parts of the Far East and South America There are variations in the clinical picture in these different areas

The parasite is round or oval from 2 to 5 μ in length and contains a large nucleus It inhabits the reticulo endothelial cells in which multiplication by binary fission takes place These cells burst the contents are released into the blood stream and further reticulo endothelial cells throughout the body are invaded

Pathology As the result of the affection of the reticulo endothelial cells the liver and spleen become greatly enlarged The haemopoietic tissue of the bone marrow is replaced by infected reticulo endothelial cells with consequent anaemia and leucopenia Enlargement of the lymph glands may occur and occasionally foci of infected reticulo endothelial cells are found in the intestines and skin which may ulcerate those in the skin forming the basis to dermal leishmaniasis The mono nuclear cells of the blood and more rarely the polymorphonuclear leucocytes are sometimes invaded

Clinical Picture The incubation period varies from a few weeks up to 3 years so the disease may not make its appearance until long after the subject has left an endemic area The onset is usually insidious with recurring febrile attacks lasting a week or so separated by remissions of varying length Sometimes the temperature is raised at night and in the afternoon with apyrexial periods in the morning and evening though regular evening fevers or irregular variations in the temperature are more common Few of the general symptoms such as nausea and headache which usually affect febrile patients accompany the fever though severe sweats are common The spleen steadily enlarges during the febrile periods and if no treatment is given may ultimately become enormous The liver also enlarges markedly but usually to a less extent Other features especially in advanced cases include diarrhoea enlargement of the lymph glands and cough and other chest manifestations (presumably as the result of involvement of the reticulo endothelial cells in the bowel glands or lungs) The skin may become dry and deeply pigmented over the cheeks (or post kala azar dermal leishmaniasis with depigmented patches macules and papules may occasionally occur a year to two after a course of treatment for kala azar) Ultimately the patient may become extremely emaciated with oedema and ascites Death may occur from bronchopneumonia other secondary infections or cancrum oris secondary to agranulocytosis Although spontaneous recovery occurs occasionally the mortality of the untreated disease is probably over 75 per cent

Anaemia and granulocytopenia begin in the early stages and later may be extreme

Diagnosis *In the early stages diagnosis is difficult* A useful clinical pointer (when present) is the double rise of temperature others are the steadily enlarging spleen and liver the remittent fever and the granulocytopenia The surest diagnostic finding is the discovery of the *L donovani* Here there can be no doubt (as there may be with malarial parasites or *E histolytica* cysts) that the parasites indicate the clinical disease though there may of course also be some other associated infection such as malaria The parasites may be found in fluid aspirated from the spleen liver marrow or lymph glands or in the peripheral blood If they are not seen on direct smears bone marrow should be cultured on Nicolle Novy and MacNeal medium By one of these means the parasites can probably be identified in

nearly every case The formal gel test may be a useful diagnostic aid A drop of commercial formalin is added to 1 ml of the patient s serum which is shaken and left for an hour at room temperature If opacity develops within this period the test is positive Nearly all subjects of kala azar show this positive test by the third month though occasionally it is also positive in other circumstances The test depends on the increase in the γ globulin fraction of the serum

Treatment Certain antimony and diamidine compounds are specific for kala azar

Sodium or potassium tartrate of antimony are widely used in endemic areas because of their cheapness but they may cause serious side-effects More satisfactory preparations are pentavalent compounds such as sodium antimony gluconate (Solustibosan) and diethylamine para amino phenylstibinate (Neostibosan) They are given intravenously in doses of 0 3–0 6 g dissolved in some 10 ml of distilled water daily for 7 to 10 days Following the course of treatment the manifestations of the Eastern form of kala azar nearly always clear up within some weeks and do not recur but antimony is much less effective for the Mediterranean form

Some of the diamidine compounds such as stilbamidine isethionate though successful have toxic effects including trigeminal and other cranial nerve palsies Pentamidine isethionate is the compound of choice side effects being rare It is given intravenously or intramuscularly in a dose of about 3 mg per kg of body weight dissolved in some 10 ml of distilled water daily for about 2 weeks It is effective for all forms of kala azar including cases which have become antimony resistant

Leprosy

Leprosy is an extremely chronic infection by the *Mycobacterium leprae* It was widespread in all parts of the world in medieval times but has now almost disappeared from most parts of Europe and fresh cases developing in Britain are unknown Before the Second World War there were said to be some 250 cases in Britain all of whom had acquired the disease abroad It is now most prevalent in the Tropics and sub tropics

Along with tuberculosis syphilis and glanders leprosy belongs to the group of infective granulomas and the *M leprae* is similar to the *M tuberculosis* The organisms are discharged in large numbers from the skin and mucous membranes of those with the lepromatous form of the disease Prolonged and intimate association with such a case is usual before the disease is transmitted In the endemic areas the great majority of infections are acquired in childhood and most adults seem to be immune Neural leprosy is thought to be non infective

Pathology In the neural or tuberculoid form of leprosy there is a vigorous reaction to the organisms which presumably have entered the body through abrasions in the skin or mucous membranes Granulomas develop on the skin and in the peripheral nerves along which the organisms find their way with consequent loss of nerve function In the lepromatous form the organisms spread to all parts of the body and multiply freely There is thickening of the skin and later widespread destructive changes Intermediate forms occur with features both of the neural and lepromatous varieties

Clinical Picture. The incubation period is difficult to assess as prolonged contact usually precedes the disease it is said to be several years as a rule and up to 20 years occasionally

The first symptoms of neural leprosy are paraesthesiae or loss of feeling usually in the distal parts of the limbs the nerves become thickened and are palpable as hard cords Sharply demarcated raised anaesthetic and depigmented areas of skin develop In lepromatous leprosy the affected skin which is at first usually that of the face and forehead becomes thickened oedematous and corrugated Subcutaneous nodules may develop which break down and ulcerate Untreated the disease advances over the course of years and is accompanied by periodic febrile attacks in which new lesions develop and there are systemic symptoms

Diagnosis. In Britain the possibility of leprosy need be considered only among people who have lived in tropical and sub tropical countries The diagnosis may be difficult in the early stages Anaesthesia is the most important finding of neural leprosy Leucoderma often causes confusion especially when there is super added hysterical anaesthesia though this may be more widespread than the affected skin or even universal Circinate fungal skin infections may at first glance suggest leprosy but the absence of anaesthesia the comparative acuteness of the process and the presence of the fungi under the microscope should make the situation clear It may be possible to recover the *M leprae* from skin biopsy but this is not always so as the organisms may be very scanty in this variety of the disease

Lepromatous leprosy may be confused with lupus vulgaris or reticuloses involving the skin It can be diagnosed by making a small incision in the infected skin taking a scraping and examining a smear stained by Ziehl Neelsen s method Numerous acid fast bacilli can be seen These can be distinguished from the *M tuberculosis* (if there is doubt as to

their identity) by the fact that they cannot be cultured or cause infection in laboratory animals

Treatment The traditional remedy for leprosy is chaulmoogra oil though its value is uncertain At present the drugs of choice are the sulphone compounds such as sulfoxone sodium (Diasone) 0 3–0 6 g daily or solapsone (Sulphetrone) 1 5–3 g daily for many months or indefinitely In mild and moderate cases these drugs will probably eradicate the disease and in advanced cases will prevent further progression and may cause considerable retrogression

CHAPTER 9

Endocrine and Metabolic Disorders

A A G LEWIS

INTRODUCTION

THE endocrine glands are ductless glands that liberate chemical substances the hormones into the blood stream Hormones are the substances produced by these glands which control the activities of other cells of the organism

Some hormones are secreted in response to a particular change in the body and their action is directed towards controlling or minimizing that change Aldosterone for instance seems to be pro duced in increased amounts in response to a fall in blood volume and acts so as to restore this Others control the rate at which certain vital pro cesses proceed Thus insulin increases the utiliza tion of glucose in the tissues and thyroxine in creases that of oxygen Hormones usually do not initiate these processes in the absence of insulin and of thyroxine some glucose and oxygen are still utilized by body cells for example

The secretion of several hormones is controlled by pituitary tropic hormones and the mutual inter action between the pituitary and the target organs provides a remarkable biological example of a "feed back control mechanism A fall in the circu lating level of a hormone leads to further produc tion of the pituitary tropic hormone and an in creased secretion by the target organ so that homoeostasis is preserved The regulation of adrenal corticoid production by corticotropin illustrates this mechanism if corticoid secretion is de creased for any reason corticotropin production is increased

One of the most fruitful concepts in endocrin ology has been that of the body s response to stress A large number of stressful stimuli such as emotion and pain trauma surgical procedures burns infections and severe fatigue have been found to evoke similar patterns of response by the endocrine system which seems to react as a unit to maintain the body s powers of resistance and homoeostasis in the face of major external in fluences These responses are largely mediated by the anterior pituitary by means of its tropic hormones changes in the rate of secretion of cortico tropin and thyrotropin leading to increased adrenal cortical activity and reduced thyroid activity respectively

The anterior pituitary itself is apparently largely controlled by the hypothalamus which in turn is linked with other centres elsewhere in the brain The endocrine system is not therefore an isolated physical mechanism it is intimately linked with the whole of the patient s vital activity and may often be the means whereby psychological events are re flected in somatic changes The oldest known example of this close relationship is the release of adrenaline in response to fear quickening the heart rate and causing vaso-constriction and pallor But an intravenous infusion of adrenaline causes a striking feeling of apprehension It is almost mean ingless to separate one event as being the primary in this case both the sensation of fear and the release of adrenaline are inseparably linked in the response of the organism to danger

In the investigation of endocrine disorders several methods direct and indirect are available for the estimation of the activity of individual glands It might be thought that a determination of the level of a hormone in the circulating blood would provide certain knowledge of this activity In practice this may not be so To know the circu lating level of a hormone at any moment does not mean that one knows the rate of its secretion into the blood stream for it may be that it is being utilized or excreted more rapidly than is normal Again the target organ may be relatively insensitive to the hormone so that an increased level may not be producing an increased effect. Even when all the separate influences affecting the rate of growth of a bone are known and can be assessed for example what is not known is why the bone responds to these influences at some stages of life and not at others very early in life it seems to have an in herent tendency to grow then for some years the growth hormone seems to stimulate this growth

while later the bone ceases to respond to this stimulus and an exceptional production of the hormone is then required to produce acromegaly

Granted these difficulties however it must be admitted that one aim of the endocrinologist is to be able to estimate the concentrations of hormones in body fluids and the rate of their production and execretion In a few cases (for example that of the adrenal glucocorticoids) the plasma levels and rate of excretion can be estimated chemically With thyroxine chemical estimations of the blood protein bound iodine with certain safeguards give a fair approximation to the circulating level of hormone But in most cases this can be found only by a bioassay which is a much more difficult procedure technically and which may give quite non specific results it the utmost care is not taken to avoid side effects The large number of claims made to have demonstrated the antidiuretic hormone in body fluids by injecting them into rats furnishes the best example of this fallacy nearly all of them are vitiated by the non specific antidiuretic effects of the procedure on the test animals

Where the hormones themselves cannot be estimated or assayed it may be possible to deduce their rate of secretion from measurement of their characteristic effects Estimation of the BMR for instance is the best example of this method for the thyroid hormone has a specific effect on oxygen utilization and heat production by body cells But often this is not possible for the hormone may be only one influence out of many that affect a particular process The rate of utilization of glucose by the tissues for example is influenced by several factors such as muscular exercise besides the local concentration of insulin and one cannot equate changes in this rate with fluctuations in the level of circulating insulin

The Pituitary Gland

Development and Anatomy The pituitary gland consists of *adenohypophysis* and *neurohypophysis* which are formed by outgrowths of ectoderm from the roof of the mouth and the floor of the 3rd ventricle respectively That from the mouth known as Rathke s pouch becomes applied to the anterior aspect of the downgrowing tissue in the fourth week of foetal life

The neurohypophysis comprises the median eminence of the tuber cinereum and the infundibular stem and process the supraopticohypophysial tracts pass into it from the supraoptic and paraventricular nuclei in the anterior hypothalamus The infundibular stem is invested by the cells of the pars tuberalis of the adenohypophysis forming the pituitary stalk A plexus of blood vessels—the pituitary portal system—surrounds this and seems to convey humoral substances downwards from the hypothalamus

The gland lies in the sella turcica of the sphenoid bone enclosed above by the diaphragma sellae a shelf of dura mater stretching between the anterior and posterior clinoid processes and pierced by the pituitary stalk The optic chiasma usually lies on the anterior part of this shelf the rest of which is in contact with the hypothalamus The cavernous sinuses lie against the outer sides of the sella

Histology The pars tuberalis and pars distalis of the adenohypophysis contain three main types of cell distinguished by their staining reactions and named eosinophil and basophil cells (chromophils) and chromophobe cells The latter seem to be in a resting state capable of development into the others which produce hormones During pregnancy the gland enlarges and its activity apparently increases many clear cells are found which seem to occupy an intermediate position in this transformation (pregnancy cells)

The neurohypophysis contains large glial cells the pituicytes round which the unmyelinated fibres of the supraopticohypophysial tracts form a terminal network

The Hormones of the Adenohypophysis

Six hormones have been isolated in a relatively pure form each having a characteristic action *growth hormone* (somatotropin) *corticotropin* (ACTH) *thyrotropin* (TSH) and the three gonadotropins *follicle stimulating hormone* (FSH) *interstitial cell stimulating* or *luteinizing hormone* (ICSH or LH) and *lactogenic* or *luteotropic hormone* (prolactin) Growth hormone is secreted by the eosinophils and the others by the basophils The tropic hormones stimulate the secretion of other endocrine glands and deficiency of the latter may lead not only to increased production of the former but also to histological changes in the adenohypophysis After removal of the gonads or of the thyroid gland there is an increase in the number of basophil cells which become vacuolated (castration cells) At the same time the number of eosinophils diminishes In adrenal deficiency the number of both eosinophils and basophils is greatly reduced In adrenal cortical hyperfunction the basophils become hyalinized and vacuolated (Crooke s cells)

Growth Hormone is a protein Experimentally it stimulates the growth of all the organs of immature animals producing positive balances of nitrogen calcium and phosphorus stimulating chondrogenesis and osteogenesis in epiphysial cartilage and increasing the appetite and weight of the organism without the storage of fat or water It stimulates the formation of glucagon by the alpha cells of the islets of Langerhans in the pancreas which in turn increases hepatic glycogenolysis while it is probably responsible for that glycotropic action of anterior pituitary extracts which opposes the formation of glucose 6 phosphate from glucose under the influence of hexokinase This opposition to the action of hexokinase is antagonized by insulin It is probable that growth hormone also stimulates the production of insulin itself its overall action in the young animal being to maintain high levels in the blood stream of both insulin and glucose so that body cells are able to take up and to utilize more of the latter as a source of energy and therefore to form new tissue from amino acids In many mature animals injections of growth hormone produce not growth but diabetes possibly because less insulin can be produced in the pancreas A further important specific function of the hormone is to stimulate fat catabolism which in itself may spare protein and carbohydrate for growth

Corticotropin (ACTH) probably a polypeptide stimulates the production of both glucocorticoids and of androgens by the adrenal cortex Its injection into hypophysectomized animals leads to an increase in the weight of this gland and a reduction in its content of cholesterol and of ascorbic acid The last action forms the basis for the commercial assay of the hormone which is prepared from animal pituitary glands and standardized in units each of which corresponds in activity to 1 mg of the original Armour standard preparation The hormone probably does not regulate the formation of aldosterone in the adrenal cortex It is rapidly removed from the blood stream and no reliable method of assay is available for clinical use

Thyrotropin (TSH) is probably a protein It appears to cause the expulsion of thyroid hormone from the thyroid follicles possibly by stimulating the activity of a proteolytic enzyme which breaks down thyroglobulin In addition hypertrophy of the cells and the formation of further hormone take place

The Gonadotropins are proteins FSH stimulates the growth of the Graafian follicles and in conjunction with LH the formation of oestrogen by the theca interna One action of oestrogen is to increase further the secretion of LH which then induces ovulation Luteotropin is responsible for the maintenance of the corpus luteum and the formation of progesterone In males FSH promotes the growth of the seminiferous tubules and spermatogenesis while LH stimulates the interstitial cells and the production of androgens

Large amounts of gonadotropin (resembling LH in its action) are formed by the placenta during pregnancy and the detection of its increased urinary excretion forms the basis of pregnancy tests Large quantities of a similar hormone are formed by the cells of chorion epitheliomas seminomas and some testicular teratomas

The placenta also produces oestrogens and progesterone This organ therefore functions as an endocrine gland to some extent replacing the anterior pituitary during pregnancy

Investigation of Pituitary Function

1 *Estimations of FSH and of TSH* in body fluids can be made in a few specialized centres Assay of the urine for FSH distinguishes between primary gonadal deficiency (in which it is greatly increased) and that due to pituitary failure (in which it is absent) This assay depends on the uterine enlargement in immature female mice brought about by injections of urinary extracts (made by alcohol precipitation or by kaolin adsorption) containing the hormone By using different dilutions of the extract rough quantitation of the rate of excretion is possible Assays of body fluids for TSH have little clinical application at present

2 *Diagnostic trials* may be carried out with ACTH and TSH in cases of adrenal and thyroid deficiency when underlying pituitary deficiency is suspected When one of these hormones produces a characteristic response on the part of the target organ it may be presumed that the normal pituitary stimulus is deficient

3 *Investigations of glucose tolerance* may be of diagnostic value

(*i*) *The Glucose Tolerance Test* (p 144) usually shows hyperglycaemia both when the subject is fasting and two hours after a glucose load in the active stages of acromegaly

(*ii*) *The Glucose Insulin Tolerance Test* 50 g of glucose are ingested at the same time that 0 1 unit of insulin per kg of body weight is injected intravenously Normally there is little rise in the blood glucose in conditions such as acromegaly and Cushing s syndrome the insulin has little effect in

modifying the rise brought about by the ingested glucose

(iii) *The Insulin Tolerance Test* An attempt is made to assess two variables—the sensitivity to insulin and the response to hypoglycaemia In the fasting normal subject the intravenous injection of 0 1 unit of soluble insulin per kg of body weight reduces the blood glucose level by 40 per cent after which the mobilization of liver glycogen restores the fasting level within two hours In the patient with hypopituitarism in the absence of the growth hormone and of the adrenal glucocorticoids the fasting level itself is below normal the injection of insulin provokes a much greater fall in this level and hypoglycaemia persists for two hours Both insulin sensitivity and hypoglycaemia unresponsiveness are therefore present The test must be carried out with great caution in suspected cases and omitted if the fasting level is much below normal Not more than one third of the regular dose should be injected and the patient should be spoken to at frequent intervals clouding of consciousness necessitates the immediate intravenous injection of glucose Blood is taken for glucose estimations 20 30 45 60 and 120 minutes after the injection of insulin

All glucose tolerance tests should be performed under standard conditions the patient being on a high carbohydrate diet for at least four days previously If the fasting blood sugar is above 130 mg/100 ml (p 144) diabetes is almost invariably present if it is below 70 mg/100 ml it may be presumed that there is some degree of hypoglycaemia unresponsiveness Levels greatly below this may be found in hypopituitarism

4 *Pituitary deficiency may be presumed* when evidence of a deficiency of more than one endocrine gland is found on investigation The combination of myxoedema with Addison s disease or with gonadal failure rarely occurs in the absence of pituitary failure Occasionally however thyroid deficiency may be so severe that there is evidence of secondary pituitary failure and thyrotropin is absent from blood stream and urine

Hyperpituitarism

Primary Hyperpituitarism The only conditions unequivocally due to the increased production of a pituitary hormone are gigantism and acromegaly which result from the secretion of excessive amounts of growth hormone by the cells of an eosinophil adenoma of the pituitary gland

When in 1932 Cushing drew attention to the association of certain abnormalities with the presence of a basophil adenoma of the anterior pituitary he recognized that they might be produced by an increased secretion of the adrenal cortex That this is the cause of Cushing s syndrome now seems to be indisputable but whether or not this may sometimes result from excessive secretion of corticotropin by the basophil adenoma of the pituitary which is frequently—though not invariably—present is not decided

An increase in the level of thyrotropin has been demonstrated in the blood of some patients with exophthalmos though not of those with hyperthyroidism without this complication The weight of evidence is against the view that Graves s disease is caused by an increased secretion of thyrotropin

Secondary Hyperpituitarism Increased rates of secretion of the anterior lobe tropic hormones occur when those of their target glands are deficient In Addison s disease the rate of corticotropin secretion is increased In gonadal deficiency there is an increase in FSH production (which may be responsible for some of the symptoms of the menopause) In myxoedema abnormally high levels of thyrotropin occur in the blood stream (without it should be noted any tendency to exophthalmos)

Gigantism

People above 6 ft 6 in in height are extremely rare and the more a person exceeds this height the more probable it is that the cause is overproduction of growth hormone by the cells of an eosinophil adenoma of the anterior pituitary To bring about excessive height this must arise before fusion of the epiphyses of the long bones Heights above 9 ft have been recorded Active growth may however continue for longer than the usual time with normal growth hormone secretion when skeletal maturation is delayed in gonadal deficiency In this case the body proportions will be eunuchoid (p 121)

Clinical Picture Gigantism usually begins at puberty which will be delayed if pressure by the adenoma on the other secreting cells of the anterior lobe leads to secondary gonadal deficiency In this case a very great height may be attained with eunuchoid proportions Otherwise the skeleton matures normally and the limbs are not disproportionate In other cases acromegalic features develop since stimulation by growth hormone may persist into adult life

Usually there is some depression of sexual func

tion and the pituitary giant suffers from muscular weakness and fatigue despite his size Enlargement of the sella turcica and visual field defects may be found as in acromegaly (q v) Death is common from intercurrent infection at an early age

Treatment An attempt may be made to reduce the activity of the adenoma by irradiation Progressive visual failure is the only indication for surgery Growth will be limited if epiphyseal closure can be brought about by sex hormones so that males should be implanted with 200 mg of testosterone every three months and females given regular doses of oestrogen Sexual activity and in the male muscular strength may be increased at the same time

Acromegaly

Marie first described this disease in 1886 deriving his name for it from the Greek words for extremity and large It results from the action of excessive amounts of growth hormone secreted by the cells of an eosinophil adenoma after the closure of the epiphyses of the long bones The adenoma slowly enlarges over many years ballooning the sella turcica beyond the extreme limits of its normal dimensions (12 mm deep and 16 mm long) and eroding the clinoid processes Pressure on the rest of the gland on the optic chiasma on the hypothalamus and ultimately on the pyramidal tracts in the cerebral peduncles may occur The increased amounts of growth hormone in the circulation stimulate the formation of periosteal new bone and the hypertrophy of cartilage muscle skin connective tissue and viscera Hyperglycaemia and glycosuria are common Enlargement of the thyroid and an increased basal metabolic rate may occur Eventually arrest of the activity of the tumour cells may occur spontaneously or as the result of haemorrhage when hypopituitarism supervenes

Clinical Picture The pressure of the enlarging tumour on neighbouring structures causes headaches which are often referred to the temples Pressure on the optic chiasma usually leads first to the degeneration of the lower of the decussating fibres from the nasal halves of the retinae so that field defects tend to appear in the upper temporal quadrants of the visual fields These may progress until bitemporal hemianopia or blindness in one or both eyes occurs The rise in intracranial pressure is insufficient and occurs too slowly to cause papilloedema so that primary optic atrophy is seen on ophthalmoscopy the optic disc appearing white and flat with sharp margins Polyuria and thirst may result from glycosuria or from pressure on the neurohypophysis Pressure on the pyramidal tracts may cause a spastic hemiplegia or paraplegia in the late stages

Periosteal new bone formation occurs in a large number of sites causing obvious enlargement of the superciliary ridges the malar bones the mandible and the bones of the hands and feet This with the hypertrophy of skin cartilage and subcutaneous tissue causes the characteristic appearance with anthropoid features large nose and tongue prognathism and large hands and feet with blunt spatulate fingers and toes The bones of the vault are seen to be thickened in the X rays of the skull with large air sinuses and an abnormally obtuse angle of the mandible while ballooning of the sella turcica and erosion of the clinoid processes are seen at an early stage X rays of the hands show tufting of the terminal phalanges with new bone those of the spine show widening of the anterior plates of the vertebrae together with loss of density due to osteoporosis

A mild polyneuritis due to involvement of the peripheral nerves in the general overgrowth of connective tissue often leads to paraesthesiae and pain in the extremities with absence of the deep reflexes

Amenorrhoea occurs in the female and impotence in the male A mild insulin resistant form of diabetes is usual though complications such as ketosis are rare Later in the disease when the activity of the cells of the adenoma is decreasing insulin sensitive diabetes occurs In spite of the goitre there are rarely any signs of hyperthyroidism

The patient may seek advice on account of headaches or of visual failure or because of the alteration in his appearance or of the need for larger shoes or gloves Impotence thirst muscular weakness or pains in the limbs may be presenting symptoms While the appearance of an established case is unmistakable there may be great difficulty in assessing early changes and reliance may have to be placed on old photographs or the evidence of relatives These may also help in deciding whether the disease is still progressing Repeated examination of the visual fields and X rays of the skeleton may then be necessary

Treatment Irradiation of the pituitary is advocated in many centres but it is doubtful whether much effect can be obtained without damaging the brain Surgical removal of the adenoma should be attempted only to save vision Testosterone therapy may improve muscular strength and sexual function in males and counteract the tendency to osteoporosis (the reason for which is unknown) Large doses of insulin may be required to control the hyperglycaemia In the later stages of the disease treatment for hypopituitarism may be necessary

Hypopituitarism

Deficiency of anterior lobe hormones may be due to compression of the secreting cells by cysts or tumours arising in *the pituitary or its immediate* neighbourhood or to destruction of these cells by inflammation fibrosis or infarction Very rarely there is a congenital deficiency of the eosinophil cells

An *adenoma of the chromophobe cells* is the commonest *of all pituitary tumours* occurring equally in both sexes usually between the ages of 30 and 50 Since the cells produce no hormones this tumour merely impairs the function of the others in the gland *Eosinophil adenomas* may compress the other cells and may themselves undergo cystic or haemorrhagic degeneration (*Basophil adenomas* often mere aggregations of these cells do not become large enough to cause pressure) *Hypophysial epidermoid tumours* (craniopharyngiomas which develop from remnants of Rathke s pouch) may arise above the sella *turcica or within it and compress* the anterior lobe *Suprasellar meningiomas* arising in adult life from the meninges around the diaphragma sellae also occasionally do so *Destruction of the anterior lobe* may be due to local abscess formation the infection reaching the sella from the sphenoidal sinus or the nasopharynx or to tuberculosis syphilis or local malignant metastases *Postpartum infarction* and necrosis may occur usually as the result of circulatory collapse after a severe haemorrhage In *severe malnutrition* associated with starvation anorexia nervosa steatorrhoea etc there may be a failure of synthesis of *some pituitary hormones* possibly as a result of a deficiency of essential amino acids

Simmonds first published an account of the necropsy of a patient suffering from atrophy of the anterior lobe in 1914 and subsequently developed his concept of pituitary failure The recognition of the importance of postpartum necrosis (described by Glinski in 1913) as a cause of this condition was largely due to the work of Sheehan whose name is given to *this particular form of the disease*

Clinical Picture The symptoms and signs of pituitary failure are present in the most striking form in a patient suffering from Sheehan s disease In *this there is usually* a history of severe haemorrhage necessitating transfusion Lactation was never established the breasts involuting while menstruation never returned The patient has become listless and apathetic appearing dreary and miserable and complaining of fatigue *of loss of appetite* and of libido and of extreme sensitivity to cold A psychosis or severe neurosis is often suspected *The skin is thin* dry and waxy white even the areolae being pale the slightly yellow tinge of myxoedema may be seen but not the pigmentation of Addison s disease All body hair disappears The genitalia atrophy and dyspareunia results libido and feminine modesty are absent Resistance to all forms of mental and physical stress is reduced infections may be rapidly fatal hypoglycaemia *and coma may occur on fasting* Coma may also be associated with a very low body temperature Loss of weight may occur but results from loss of appetite and indifference or to tuberculosis severe wasting is rare There is a normochromic anaemia

Slowly growing tumours destroy the anterior lobe and produce pituitary deficiency much more insidiously In adults sexual failure is usually the first symptom in children failure of growth or delayed sexual maturation Often there is timidity and loss of confidence in males so that a neurosis is suspected Later thyroid and adrenal deficiency *develop and the complete clinical picture of* panhypopituitarism emerges In some patients the most striking deficiency is that of the thyroid and a diagnosis of myxoedema is made when its true nature is recognized this condition is known as *pituitary myxoedema*

When a tumour is the cause symptoms may arise from pressure on surrounding structures headache visual field defects and polyuria Diabetes insipidus however develops only from posterior *lobe destruction* in the presence of some anterior lobe function it may therefore occur only as a temporary complication in the progressive development *of panhypopituitarism*

Diagnosis Sheehan s disease can usually be diagnosed from the appearance of the patient *and from* her history The sexual failure and the signs of myxoedema yet without pigmentation or body hair are diagnostic and occur in *all fully developed cases* of panhypopituitarism Chromophobe adenomas cause enlargement of the sella and often visual disturbances before there is much *evidence of glandular failure* and even without any craniopharyngiomas show some calcification on X rays in 75 per cent of cases

The diagnosis of partial pituitary failure may be difficult to establish it must rest upon evidence of deficiency of more than one endocrine *gland or* upon failure of growth or of sexual function with an abnormal insulin tolerance test It is the adrenal deficiency of hypopituitarism that is frequently overlooked for the electrolyte regulating function of the cortex is preserved the blood pressure and blood electrolyte levels may be normal and pigmentation is absent The thyroid deficiency on the other hand

is often immediately obvious though sexual failure loss of weight or an anomalous ^{131}I uptake or response to thyroid therapy may all suggest its pituitary origin

The laboratory investigations that may be required to establish the diagnosis may therefore be the insulin tolerance test the estimation of the 24 hr excretion of 17 ketosteroids (less than 1 mg in all severe cases) the Robinson Power Kepler test and the estimation of the BMR and ^{131}I uptake (which may give conflicting results) In many cases a short course of injections of TSH or ACTH may establish that the target glands can ultimately respond to stimulation

The condition most commonly mistaken for hypopituitarism is anorexia nervosa The patient is often a young woman who in spite of her emaciation appears mentally and physically active Body hair is preserved The 17 ketosteroid excretion may be somewhat reduced but the insulin tolerance test is normal

Treatment Operations are indicated on cysts or tumours only to save vision they may be followed by the loss of any pituitary function that remains Injections of growth hormone are not beneficial Thyroid should be given with great care for a small dose may precipitate an adrenal crisis on the other hand resistance to it is not uncommon Cortisone must be given whenever there is evidence of adrenal deficiency and produces a striking improvement in the patient s activity sense of well being and ability to stand all forms of stress Extra salt and injections or implants of DOCA are rarely necessary Testosterone may be given to both sexes to promote protein anabolism oestrogen may be given to prevent genital atrophy in females

A high carbohydrate diet avoidance of fatigue exposure and fasting and the early and vigorous treatment of infections are all necessary Coma requires the immediate intravenous infusion of glucose and since it is often precipitated by infection injections of crystalline penicillin Recovery from coma with hypothermia has occurred after immersion in a warm bath

Body Growth

Normal growth proceeds until about the age of 18 though the rate is greatest at puberty At birth the limbs are short in relation to the trunk the ratio of the length of the body above the symphysis pubis to that below being 1 7 1 By 10 years of age this ratio has fallen to unity when the span of the arms is equal to the height After this age the skeletal proportions remain constant As the skeleton matures centres of ossification appear at definite times Ultimately the epiphyses fuse and growth is ended since this occurs earlier in girls than in boys they tend to be the shorter If maturation is delayed but growth continues (as in eunuchs) the limbs become disproportionately long so that the span is greater than the height and the symphysis pubis relatively nearer the head In assessing growth therefore the bone age (judged by X ray evidence of the state of the epiphyses and the appearance of the centres of ossification) and the body proportions have to be considered as well as the actual height

For normal growth there must be an adequate supply of protein fat carbohydrate vitamins and mineral salts in the diet and intestinal absorption must be normal also Essential aminoacids must be available both for the formation of tissue and for the synthesis of hormones and fat and carbohydrate metabolism must supply sufficient calories to prevent these aminoacids being diverted to energy production

Absence of growth hormone leads to dwarfism Over production by the cells of an eosinophil adenoma leads to gigantism in early life and to acromegaly once the epiphyses have united Normal thyroid function is also necessary for growth (though the hormone does not directly stimulate it) and for skeletal maturation the cretin is not only stunted but retarded in his bone age Sex hormones stimulate growth but eventually limit it by causing fusion of the epiphyses and skeletal maturation Pituitary dwarfs may therefore continue to grow slowly throughout life if sexual maturation never occurs

Dwarfism may be primordial or due to progeria thyroid deficiency pituitary deficiency ovarian agenesis achondroplasia or chronic disease

1 Primordial dwarfs are normal in every respect apart from their short stature There is no mental or endocrine abnormality and they mature normally There is no familial tendency

2 Progeria is a rare progressive fatal disease in which dwarfism premature senility and baldness occur Severe mental defects are usual The cause is unknown

3 In hypothyroidism multiple foci of ossification occur in the epiphyses (stippling ') and skeletal maturation is retarded The blood cholesterol is raised and the ^{131}I uptake subnormal

4 Pituitary dwarfism is usually due to destruction of the anterior lobe by a craniopharyngioma or less commonly by a chromophobe adenoma Very rarely there is an isolated failure of the eosinophil cells The body proportions remain normal There is nearly always a failure of sexual development as well and in males the testes may not descend Intelligence is normal but emotional immaturity is the

rule The term infantilism is commonly used for this syndrome Laboratory investigations show a low BMR low 17 ketosteroid and FSH excretion and an abnormal insulin tolerance test

5 In ovarian agenesis moderate dwarfism is the rule the patients often being about 4 ft 7 in tall FSH excretion is increased There may be other stigmata of Turner s syndrome (p 141)

6 In achondroplasia there is a family history and the abnormally short limbs are characteristic

7 Many chronic diseases in childhood are associated with a reduced rate of growth notably congenital heart disease renal disease and chronic infections It is most important to recognize intestinal malabsorption (due to fibrocystic disease of the pancreas to coeliac disease or to steatorrhoea) because of the importance of early therapy

Treatment Preparations of growth hormone have not been effective in stimulating growth But endocrine deficiencies must be corrected wherever possible In pituitary dwarfism courses of chorionic gonadotropin (500 I U 3 times a week for 2 months followed by a 2 month interval) should be given Testosterone will also stimulate growth provided the dose is insufficient to cause skeletal maturation

Sexual Maturation

At puberty the activity of the adrenal cortex and the gonads increases In both sexes excretion of FSH in the urine can be detected while the urinary 17 ketosteroids (which begin to rise appreciably after the age of 8) approach the adult level In females the growth of body hair is stimulated by the adrenal androgens while oestrogen (now detectable in much greater quantities in the urine) promotes enlargement of the breasts labia minora vagina and uterus The sex hormones stimulate skeletal growth and then the closure of the epiphyses in both sexes In males androgens are produced both by the testes and by the adrenals leading to growth of the penis scrotum and prostate to enlargement of the larynx to increased growth and strength of the muscles and to masculine drive aggressiveness and libido

The menopause occurs when the ovarian hormones are no longer secreted Gonadotropins are formed and excreted in the urine in increased amounts Many women suffer from hot flushes or flashes (sudden sensations of heat which may involve the head or the whole body) giddiness headaches irritability and other symptoms which can be largely prevented by small regular doses of oestrogen

The Neurohypophysis

The pituicytes of the neurohypophysis secrete antidiuretic hormone (ADH vasopressin) and oxytocin The secretion of ADH is stimulated by a rise in the tonicity of extracellular fluid acting on specialized cells (the osmo receptors) which may lie in the anterior hypothalamus ADH stimulates the renal tubular re absorption of water from the glomerular filtrate reducing the volume of the urine and increasing its concentration Water can thus be conserved by the organism or if the tonicity of ECF falls rapidly excreted (p 154) The secretion of ADH is also stimulated by a fall in the volume of the left auricular contents so that vascular collapse and reduced blood volume or ECF volume are associated with oliguria Emotional disturbances and certain drugs such as nicotine and morphine also stimulate the secretion of ADH

Diabetes Insipidus

This has been described as A long continued abnormally increased secretion of non saccharine urine not caused by renal disease (Frank 1794) The condition results from the failure of secretion of ADH usually after destruction of the posterior lobe or anterior hypothalamus by primary or secondary neoplasms by sarcoidosis by syphilitic or tuberculous meningitis by xanthomatous deposits in the Hand Schuller Christian syndrome or by encephalitis It may develop after head injuries and occasionally degeneration of the supraoptico hypophysial tracts occurs In many so called idiopathic cases the cause remains unknown Very rarely the disease is caused by a defect of the renal tubules which do not respond to ADH this nephrogenic form is familial

Clinical Picture There is constant polyuria leading to severe thirst The urine is normal but of low specific gravity and urological investigations are negative The fact that an injection of pitressin tannate produces a normal urine volume and concentration eliminates the diagnosis of nephrogenic diabetes insipidus and of water losing nephritis Occasionally however the patient is actually suffering from polydipsia which is an hysterical manifestation (although a thirst centre probably exists in the hypothalamus primary disturbances of the thirst mechanism must be exceedingly rare) This condition can be differentiated from true diabetes insipidus by (*i*) a dehydration test in which urine specific gravity rises progressively above 1 010 This may be an intolerable procedure for a patient with the organic disease though even in this case the urinary S G may rise to 1·010 or slightly more as the functioning tissue in the posterior lobe is seldom completely destroyed (*ii*) a rapid intravenous infusion of 2 5 per cent saline to produce hypertonicity of ECF (*iii*) an intravenous infusion of 3–9 mg of nicotine acid tartrate or the

inhalation of cigarette smoke until nausea and malaise indicate the absorption of a corresponding quantity of nicotine All these procedures stimulate the secretion of ADH in the neurohypophysis in a case of polydipsia and the urine may be concentrated for several hours Much smaller more transient responses occur in diabetes insipidus

Treatment Replacement therapy by 5 U pitressin tannate intramuscularly controls the polyuria for 24–72 hr The patient should not drink much fluid in this time for it cannot be excreted normally and overhydration may occur it is a useful guide to follow the body weight Control for shorter periods can be obtained by pituitary snuff

The Adrenal Glands

Each adrenal gland consists of a medulla which is surrounded by a cortex composed of three layers of cells named the zona reticularis zona fasciculata and zona glomerulosa from within outwards The cortex which develops from mesoderm is penetrated early in foetal life by masses of phaeochromoblasts developing from sympathetic ganglion cells and ultimately forming the chromaffin cells of the medulla

The Hormones of the Adrenal Cortex

Twenty nine steroid hormones have been isolated from the adrenal cortex All are derived from the cyclopentanoperhydrophenanthrene nucleus (Fig 9 1) the rings of which are designated A B C and

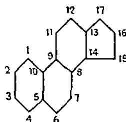


FIG 9 1 CYCLOPENTANOPERHYDROPHENANTHRENE NUCLEUS

D and the carbon atoms numbered as shown The majority contain 21 carbon atoms One (oestrone) has only 18 These corticoids comprise four groups—

1 *Glucocorticoids* containing an oxygen atom or hydroxyl group attached to carbon atom 11 (11 oxysteroids) Four of them exist named Compounds A B (corticosterone) Fig 9 2 E (cortisone 11 dehydro 17 hydroxycorticosterone) and F (hydrocortisone cortisol) Fig 9 3 The last is the only one secreted in large amounts by the adrenal cortex of man and the rate at which this occurs is regulated by the pituitary secretion of corticotropin The latter probably stimulates the conversion of cholesterol to progesterone which is turned via 17 hydroxyprogesterone into cortisol Administration of cortisone or of cortisol in turn depresses the production of corticotropin

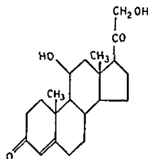


FIG 9 2 CORTICOSTERONE

These compounds maintain the level of the blood glucose by promoting its formation from amino acids (gluconeogenesis) thereby diverting them from protein anabolism and increasing nitrogen excretion They maintain the liver glycogen stores and oppose the action of insulin in the tissues They promote renal tubular sodium re absorption from the glomerular filtrate and decrease that of potassium though to a far smaller degree than does aldosterone They maintain glomerular filtration rate and renal blood flow and the ability of the renal tubules to elaborate large volumes of dilute urine in response to a water load They bring about an increase in the number of circulating granulocytes but reduce that of lymphocytes and eosinophils They modify many inflammatory responses

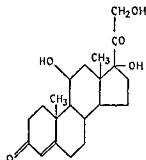


FIG 9 3 17 HYDROXYCORTICOSTERONE (COMPOUND F CORTISOL)

particularly those that are allergic in nature while causing an increased circulation of antibodies and reducing the permeability of synovial membranes

2 *Mineralocorticoids* These compounds exert a relatively much greater action on sodium and potassium excretion than do the glucocorticoids with a much weaker glucose regulating activity They promote sodium retention and potassium excretion by the kidney and hence tend to maintain the extracellular fluid volume and therefore the blood volume cardiac output and blood pressure Desoxycorticosterone and aldosterone both possess these properties though only the latter is formed in the human adrenal cortex, probably independently of stimulation by corticotropin

3 *Androgens* Under the influence of ACTH the cortex forms several hormones with androgenic activity others being formed in the course of the metabolism of other corticoids These substances are 17 ketosteroids (with a ketone group attached to carbon atom 17 Fig 9 4) and are excreted in the urine According to the orientation of the oxygen atom attached to carbon atom 3 they are divided into alpha and beta compounds The latter derive only from the adrenals the alpha compounds are formed from testicular androgens as well

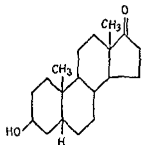


FIG 9 4 ANDROSTERONE

4 *Oestrone and Progesterone*

Regulation of Adrenal Cortical Secretion There is some evidence that aldosterone secretion is regulated directly by changes in the intake of sodium and potassium and in extracellular fluid volume being stimulated by a need to conserve sodium and ECF This regulation bears a close relationship to that of the antidiuretic hormone of which the secretion is stimulated by a rise in ECF sodium concentration (acting via the osmoreceptors in the hypothalamus) and by a fall in ECF volume (when this is reflected by a fall in the volume of blood returning to the left auricle) The two hormones therefore act together to regulate ECF volume and tonicity and thereby partly control those of the intracellular fluid also

Glucocorticoid activity is regulated by the level of circulating corticotropin and in turn largely controls it Under many conditions of emotional and physical stress particularly those associated with injuries burns and infections there is an increased utilization of these corticoids by the tissues the resulting increase in corticotropin secretion being perhaps boosted further by humoral agents such as adrenaline and by emotional stimuli acting on the hypothalamus

The adrenal androgens are formed in increased amounts during corticotropin stimulation of the cortex but do not depress the secretion of the pituitary hormone A disorder of metabolism of the adrenal cortex such as occurs in the adrenogenital syndrome in which androgens are formed instead of glucocorticoids may therefore result in further stimulation of the gland When an adrenal cortical tumour mainly produces androgens atrophy of the other adrenal cortex does not occur since corticotropin secretion continues but when it produces glucocorticoids the latter is suppressed and contralateral adrenal atrophy is common

Investigation of Adrenal Cortical Activity *The chemical estimation of individual corticoids* is an elaborate procedure possible in very few laboratories

The 17 hydroxycorticosteroids can be estimated in plasma and in man this is tantamount to estimating cortisol The normal level varies slightly according to the method used average figures being 3–20 μg/100 ml A low level is found in Addison s disease and an increased one after surgery burns and injuries after corticotropin administration to patients with normally functioning adrenal cortices and in Cushing s syndrome Under similar conditions an increase in the urinary excretion of these compounds can be demonstrated

The 24 hr urinary excretion of neutral 17 ketosteroids is widely used as an index of cortical activity These compounds are estimated after extraction colorimetrically by the Zimmerman reaction with *m* dinitrobenzene using androsterone as a standard of reference The excretion ranges from 10–25 mg/24 hr for men and from 5–20 mg for women Up to 7 years of age it is normally less than 1 mg during the next 5 years of life it rises to 4 mg and by 15 years reaches 8 mg on the average The excretion in Addison s disease in females and in panhypopituitarism is very low usually less than 1 mg It is also reduced in anorexia nervosa malnutrition myxoedema and some infections and chronic diseases Increased excretion occurs in hyperplasia and tumours of the adrenal cortex and

after stimulation by corticotropin There is a greatly increased formation of β-17 ketosteroids in carcinomas of the adrenal cortex these can be separated from the alpha fraction by precipitation by digitonin and estimated separately The principal hormone in this group dehydroisoandrosterone gives a positive colour reaction with concentrated sulphuric acid (the Patterson reaction) A slight increase in the excretion may occur in virilism associated with arrhenoblastomas or adrenal rest tumours of the ovaries or with polycystic ovaries An enormous increase may be produced by a Leydig cell tumour of the testis

The response to the administration of corticotropin may be determined when adrenal cortical deficiency is suspected The following methods are available—

1 Stimulation by the injection of 25 I U of ACTH Normally the eosinophil count in the blood falls by more than 50 per cent 4 hr later This response is not specific and should be used only as a rapid indication of probable adrenal activation

2 Stimulation by the intravenous infusion of 25 I U of ACTH in saline during 8 hr on each of 2 successive days or by 2 daily injections of 80 I U of ACTH gel Normally there is a rise of 4 mg in the excretion of 17 ketosteroids and of corticoids in the second 24 hr

The Robinson Power Kepler Test is one which summates four separate abnormalities found in adrenal deficiency namely lowered urea clearance increased chloride clearance nocturia and impaired diuretic response to a water load Urine is collected from 10 30 p m to 7 30 a m and the volume measured 20 ml water per kg body weight are then drunk in 30 min and urine collected every hour for 4 hr If the volume of any one of these exceeds that of the night urine the procedure is negative and Addison s disease excluded If this is not the case a factor is derived which equals

$$\frac{\text{vol of largest day specimen}}{\text{vol of night urine}} \times \frac{\text{plasma chloride}}{\text{urinary chloride}} \times \frac{\text{urinary urea}}{\text{plasma urea}}$$

The chloride and urea concentrations are in mg/100 ml and estimated on blood taken at the end of the test and on the night urine sample If this factor is greater than 30 the patient probably does not have Addison s disease if less than 25 he probably has it if nephritis is excluded

Adrenal Cortical Hyperfunction

The activity of the adrenal cortex normally increases as puberty approaches An increase in activity occurs under conditions of stress to which it may be regarded as a normal response and during the administration of ACTH

A pathological increase might be expected to lead to one of four disorders according to the type of corticoid formed in excess or to some combination of them These four disorders are now clearly recognized and defined as follows—

1 Cushing s syndrome due to excessive secretion of glucocorticoids

2 The adrenogenital syndrome due to the androgens

3 Primary aldosteronism or Conn s syndrome

4 Feminization in males a very rare condition

All four of the above abnormalities have occurred in association with adrenal cortical tumours while the first two may be due to cortical hyperplasia or to adrenal cortical rest tumours of the ovaries Occasionally they are associated with diseases of other organs

Some overlapping between these conditions is common varying degrees of virilism occur in females with Cushing s syndrome and *vice versa* while some feminization is common in males with Cushing s syndrome

Cushing s Syndrome

Cushing gave the first clear description of this condition in 1932 and although he realized that adrenal over activity might be the immediate cause he ascribed it to the activity of a basophil adenoma of the anterior pituitary The latter however is by no means always present. There may be no demonstrable abnormality of the adrenal cortex or hyperplasia of the gland or an adenoma or carcinoma may occur Rarely there is a tumour of adrenal rest cells in the ovary Carcinoma of the thymus and of the bronchus have been associated with this syndrome It is commoner in females than in males and may occur at any age

Clinical Picture The patient may first complain of an altered appearance or of the recent development of easy bruising or of painful obesity of tiredness and muscular weakness or of impotence or amenorrhoea

The appearance is characteristic the face being fat and often a dusky red colour The fat cheeks give the mouth a sun fish appearance and hide the ears when the patient s face is observed from

the front Women tend to develop facial hair and acne The body is obese, and the pendulous abdomen contrasts with the wasted muscles of the buttocks and thighs Livid purple striae atrophicae are often seen on the lower abdomen and there is a pad of fat over the lower cervical spine

The skin is thin and the plethoric appearance is partly due to the ease with which the smaller vessels are seen the occurrence and colour of the striae are due to the same cause Bruises may be seen after slight trauma purpura and spontaneous ecchymoses are common Hypertension is the rule and there may be papilloedema Women show varying degrees of virilism Some oedema is common

There is often a moderate increase in the haemoglobin and red cell count with a tendency to leucocytosis lymphopenia and eosinopenia The plasma potassium may be low with the low chloride high bicarbonate and tendency to alkalosis seen with potassium deficiency The blood sugar is also raised and the response to a glucose load with and without insulin may indicate insulin resistant diabetes X rays of the skeleton may show osteoporosis and spontaneous fractures The blood and urine levels of 17 hydroxycorticosteroids are increased as may be the urinary excretion of 17 ketosteroids The last is often in the normal range

Mental changes and emotional instability are frequent Mania may occur depression and suicidal tendencies are common

The abnormalities that occur in Cushing s syndrome can be ascribed to over activity of the adrenal corticoids particularly cortisol Increased gluconeogenesis probably reduces the supply of amino acids for the replacement of tissue protein so that deficiency of the protein matrix of bone and skin causes the skeletal and cutaneous changes and muscular wasting occurs in the same way The increased renal potassium loss causes a deficiency which increases the muscular weakness In women the abnormal androgenic activity causes hirsutism acne enlargement of the clitoris and amenorrhoea

Diagnosis This is made from the appearance in the great majority of patients Not all the features of the syndrome are present in every case but the diagnosis should if possible be confirmed by estimation of the blood level or urinary excretion of 17 hydroxycorticoids

Clinical Course The prognosis without treatment is very bad the majority of patients dying within a few years of intercurrent infection or of malignant hypertension About 20 per cent have malignant adrenal tumours Surgery is therefore advisable whenever facilities are available

Treatment Exploration of both adrenals followed by total adrenalectomy or removal of an adrenal tumour is the safest procedure The patient should be given 200 mg cortisone i m daily for 5 days starting 2 days before operation 100 mg cortisol is given by slow infusion during the operation On the succeeding days the dose is progressively reduced according to the patient s progress

Acute post operative vascular collapse is the most dangerous complication and is especially liable to occur when a benign tumour is removed since the other adrenal may be atrophic and in effect the adrenalectomy is then complete This collapse should be treated by intravenous hydrocortisone and an infusion of noradrenaline

The Adrenogenital Syndrome

When the most striking effect of adrenal cortical over activity is a change in the physical sexual characteristics of the patient the condition is termed *the adrenogenital syndrome* At all ages this is more common in females The virilizing stimulus is the increased production of adrenal androgens either by the cells of a cortical tumour or by a gland which seems to be incapable of forming cortisol from 17 hydroxyprogesterone In the latter case pregnanetriol is formed instead and excreted in the urine while the production of corticotropin no longer inhibited by cortisol is increased stimulating cortical hyperplasia and the formation of androgens

The abnormal stimulus may occur early in foetal life when it is much commoner in females and is usually due to cortical hyperplasia the result being female pseudohermaphroditism (that is the child has ovaries but its sex is difficult to determine by examination) In children there is usually a cortical tumour which is more often malignant than benign precocious puberty occurs in boys and heterosexual precocity in girls In adult females cortical hyperplasia is commoner than tumour and causes virilism In both children and adults some features of Cushing s syndrome may occur though the adrenogenital syndrome is much commoner without these than is Cushing s without evidence of virilism in females In infants however especially in males there is often evidence of deficiency of other cortical functions

Female Pseudohermaphroditism The foetal gonad begins to develop into an ovary in the tenth week If the abnormal stimulus develops after this further differentiation occurs along masculine lines with persistence of the urogenital sinus the vagina then opens into the urethra or the two have a common orifice The clitoris is enlarged and a scrotum may form by fusion of the labial folds but no descent of the gonads occurs The child is born a pseudohermaphrodite (True hermaphroditism with an ovo testis is extremely rare and is a genetic

abnormality) After birth further virilization occurs so that body hair growth deepening of the voice and enlargement and erections of the phallus may occur in the first few years of life Bone growth is stimulated but fusion of the epiphyses occurs earlier than normal limiting further growth The normal changes of puberty in females are suppressed

The adrenogenital syndrome in children is com moner in females in whom there is hirsutism en largement of the clitoris and rapid growth followed by early epiphysial closure Rarely there is true precocious puberty in females (isosexual precocity) In males all the signs of puberty are found apart from enlargement of the testes and spermatogenesis There is considerable muscular development and libido occurs In both sexes many of the features of Cushing s syndrome may be found and obesity or hypertension may in fact be the chief abnormalities Tumour of the adrenal usually malignant is a commoner cause than hyperplasia The 17 keto steroid excretion is raised malignant tumours secrete large quantities of the beta fraction particularly of dehydroisoandrosterone which gives a positive Patterson reaction

Virilism in Adult Females Hypertrichosis acne amenorrhoea atrophy of the breasts and enlarge ment of the clitoris occur The physical form be comes masculine and sometimes the sexual inclina tion also The voice deepens Sterility is the rule Varying degrees of Cushing s syndrome may be associated with this condition Adrenal hyperplasia is a commoner cause than tumour The urinary ex cretion of 17 ketosteroids is usually increased especially when a malignant tumour is the cause

Diagnosis Pseudohermaphrodites should be sub mitted to urethroscopy when the vaginal opening can be seen a radio opaque dye should be injected to demonstrate the Fallopian tubes

In infants the condition may present as one of adrenal cortical deficiency with vomiting diarrhoea wasting and circulatory collapse The presence of sodium and chloride in the urine in spite of the alimentary losses is an important diagnostic point

In both children and adults it is necessary to distinguish between adrenal hyperplasia and tumour The injection of 100 mg cortisone a day by suppressing the production of ACTH will rapidly reduce the urinary excretion of 17 keto steroids to normal levels when the cause is hyper plasia No effect is observed when there is an adrenal tumour The high level of excretion of the beta fraction also favours the latter

Virilizing ovarian tumours may be difficult to diagnose In the majority ketosteroid excretion is normal or only slightly increased and virilization is not intense The commonest condition is that of sclerocystic ovaries both of which may be palpable

Treatment. Surgery is indicated for virilizing tumours of the adrenals and ovaries when some degree of regression of the virilism may occur

Adrenal cortical hyperplasia should be treated with cortisone preferably by injection the dose being regulated to produce constantly normal 17 ketosteroid excretion In female pseudoherma phrodites a plastic operation on the vagina may still be necesary However where the child has already been brought up as a male it is probably wiser not to interfere at all

Emergency treatment for adrenal cortical defici ency by intravenous hydrocortisone and glucose saline and intramuscular DOCA may be required

Sexual Precocity

This may be considered to be present if puberty seems to take place before the age of ten years Actually spermatogenesis and ovulation occur only in one form of the condition and libido is unusual The causes may be classified as follows—

1 *Cerebral* This the only group in which true puberty occurs is the largest In *constitutional precocity* no other abnormality is present this is very rare in males and there is a definite familial tendency Puberty has occurred in the first few months of life and pregnancy in the fourth year

In other cases in this group there is an abnor mality in the posterior hypothalamus resulting from encephalitis or meningitis from pressure from the floor of the third ventricle a pineal tumour or the lesions of neurofibromatosis tuberose sclerosis or polyostotic fibrous dysplasia The lesion probably removes an inhibition normally exerted on the hypothalamus

2 *Adrenal* Iso sexual precocity very rarely results from adrenal cortical tumour in females In males in spite of the large penis the testes are small and spermatogenesis does not occur The 17 ketosteroid excretion is raised (p 124)

3 *Gonadal* Leydig cell tumours of the testis (p 141) are very rare Granulosa cell tumours of the ovary may cause precocity in girls by which time they are always palpable They may be bilateral

Treatment Where there is no question of remov ing a tumour the less that is done the better Con stitutional precocity needs tactful handling and explanation but a girl must be supervised as preg nancy is possible

Primary Aldosteronism (Conn s Syndrome)

This is a rare condition usually caused by a cortical adenoma The increased secretion of aldo sterone leads to sodium retention (though without

oedema) hypertension and potassium depletion The latter may cause muscular weakness or paralysis paraesthesiae polydipsia and polyuria and hypokalaemic nephropathy (p 155) for which the syndrome is often mistaken It has been suggested that the absence of a potassium diuresis after administration of cortisone or of ACTH may confirm the diagnosis otherwise this rests on the findings of increased blood and urine levels of the hormone (an estimation which can be undertaken at very few centres) and of a cortical tumour or hyperplasia at exploratory operation

Adrenal Cortical Hypofunction

A deficiency of adrenal cortical hormones occurs when the cortex is destroyed by malignant deposits (which though common rarely destroy both glands) by tuberculosis or by simple atrophy All secretions of the cortex are suppressed The condition was described by Thomas Addison in 1859 and is known as *Addison s disease* A very acute form of adrenal deficiency may occur in infants after birth trauma and with fulminating septicaemia (usually meningococcal) in both children and adults This is known as the *Waterhouse Friderichsen syndrome* Adrenal deficiency is now produced surgically by the operation of total adrenalectomy for Cushing s syndrome and malignant hypertension and in an attempt to control the growth of certain malignant neoplasms

Adrenal cortical deficiency also occurs secondarily to the failure of corticotropin production in panhypopituitarism In this case aldosterone secretion largely continues and many of the features of Addison s disease are not seen It is probable that mild forms of adrenal deficiency particularly of glucocorticoid production occur and are difficult to detect A group of patients suffering from vague ill health and reduced resistance to stress with symptoms similar to those of neurotics has been described the response to stimulation by ACTH was subnormal It seems possible that some of these may ultimately develop Addison s disease

Addison's Disease

Clinical Picture The onset is extremely insidious with vague ill health lack of energy stamina and resistance (often thought to be neurotic symptoms) progressive pigmentation unexplained attacks of vomiting and diarrhoea or hypotension and postural syncope Occasionally the onset is acute particularly after an infection which may precipitate an Addisonian crisis Such a crisis usually takes the form of vomiting diarrhoea and progressive circulatory collapse but other forms do occur There may be sudden unexplained collapse with prolonged hypotension or coma or paroxysms of abdominal pain may occur *The pigmentation is characteristic* a general deposition of melanin occurs especially on exposed areas in scars and on pressure lines it is increased by exposure to sun light and often contrasts with clear cut areas of vitiligo Pigmentation of skin folds such as the palmar creases occurs and is seen also in the buccal mucous membrane Almost black spots of intense pigmentation may be found especially on extensor surfaces

The Cardiovascular System The symptoms and signs are those of low ECF volume and hypotonicity (p 155) The systolic blood pressure is below 100 mm Hg postural hypotension is common and syncope may occur the chest X ray shows the heart to be small The plasma sodium concentration is subnormal (less than 130 mEq/litre) and the potassium may be raised In spite of these findings the urine contains normal amounts of sodium It is possible that some of the symptoms such as headache nausea and vomiting are due to water intoxication and cellular overhydration There is no diuretic response to the ingestion of a water load large volumes of urine may be formed at night and it seems that only this nocturia prevents the invariable development of water intoxication

The Nervous System Headache convulsions and coma may occur and Addisonian crisis may be mistaken for epilepsy encephalitis or a cerebral vascular catastrophe Muscular weakness and extreme fatigue are common symptoms

Other Systems Hypoglycaemia may develop on fasting Unexplained nausea vomiting and diarrhoea are common Infections are poorly resisted and may be fatal The metabolism is reduced though the BMR is usually in the low normal range

Diagnosis Many of these patients are regarded as being neurotic until some unmistakable sign is found The pigmentation usually though not always develops early in the disease and may precede all other signs by years Pigmentation in the mouth is almost pathognomonic it occurs very occasionally in coloured races and may develop after the ingestion of bismuth silver or arsenic The combination of the signs of low ECF volume and low plasma *sodium concentration with normal or raised* urinary excretion of sodium occurs only in Addison s disease and salt losing nephritis The tests of

adrenal cortical function—the 17 ketosteroid excretion the Robinson Power Kepler test and the response to ACTH (p 125) confirm the diagnosis

Clinical Course This is invariably downwards without treatment often a patient who seems to have maintained a precarious position for some months or years suddenly deteriorates and dies rapidly in a crisis or this may be provoked with little previous warning by an infection Tuberculosis in the Addisonian patient may progress or even first come to light after therapy but in the majority of cases of tuberculous aetiology the infection has been overcome before adrenal deficiency develops With modern therapy the prognosis is good and many patients live almost normal lives

Treatment Addisonian crisis calls for immediate and vigorous therapy It is essential to restore ECF volume and as much as 7 litres of physiological saline may be needed intravenously The first litre which should be hypertonic may be given rapidly Glucose is also required but as the ECF is already hypotonic and the kidney may be unable to excrete water normally it should be given by mouth or as a hypertonic solution 100 mg of cortisol should be given by intravenous infusion during every 4 hr If there is a delay in the rise of the blood pressure after therapy has begun a noradrenaline infusion must be maintained To reduce the excessive loss of sodium in the urine 10 mg of DOCA are injected intramuscularly b d Since a crisis is so often precipitated by infection a million units of soluble penicillin may be given 6 hourly intramuscularly or intravenous chlortetracycline added to the saline infusion

Once the crisis has been controlled maintenance therapy is continued with oral cortisone which should be given twice or three times a day in a dose of 12 5 mg Many patients do better with extra salt in the diet and the renal salt retaining activity of cortisone may be reinforced by fludrocortisone acetate (9 alpha fluoro hydrocortisone acetate) 0 1 to 0 2 mg daily It should be possible to maintain the patient s blood pressure and ECF sodium and potassium at normal levels by this means giving enough cortisone to restore a sense of well being and normal activity and appetite The dose of cortisone should be promptly increased by the patient himself if any infection develops If surgery becomes necessary an intramuscular depot of 200–500 mg of cortisone should be injected 48 hr before operation if the latter is an emergency procedure 100 mg of cortisol should be given as an intravenous infusion and repeated at increasing intervals

A watch should be kept for evidence of active tuberculosis which should be treated along the usual lines (p 353)

The Waterhouse Friderichsen Syndrome

There is high fever abdominal pain and severe headache are complained of a purpuric rash and livid cyanosis are seen and there may be diarrhoea vomiting convulsions and circulatory collapse The condition is rapidly fatal unless immediate treatment is given with penicillin and intravenous saline and cortisol

The Adrenal Medulla

The cells of the adrenal medulla secrete both adrenaline and noradrenaline The former stimulates the heart increases the cardiac output and heart rate and causes a rise in systolic blood pressure but it dilates the coronary and muscle blood vessels while constricting those elsewhere causing a fall of diastolic pressure It stimulates glycogenolysis and therefore causes a rise of blood sugar Noradrenaline which is also the chemical transmitter at sympathetic nerve endings reflexly slows the heart rate and has a uniform vaso-constrictor action raising both systolic and diastolic blood pressures

Tumour of the Adrenal Medulla (Phaeochromocytoma)

This tumour is composed of phaeochromocytes and therefore produces abnormally large amounts of the two adrenal medullary hormones Some tumours are malignant though this cannot be diagnosed from their histology alone as mitosis may be seen in the cells of benign tumours About 10 per cent are bilateral and about one third are palpable They may produce paroxysms of hypertension by liberating large quantities of the hormones into the blood stream or chronic hypertension with or without severe exacerbations may occur Massage of a palpable tumour or handling it at operation may precipitate an attack

In the attacks the patient is conscious of a throbbing headache and palpitation and often of nervousness sweating and flushing and of nausea vomiting and abdominal pain The metabolism is often increased and diabetes may occur

Diagnosis The tumour may be palpable or one kidney may be displaced in the pyelogram or perirenal air insufflation may indicate a tumour The combination of hypertension with hyperthyroidism and diabetes is always suggestive of this condition

Confirmation that the hypertension results from the circulation of noradrenaline should be sought from direct assay of the urinary output of this

hormone and of adrenaline now possible at several centres The effect of the injection of an adrenolytic drug should also be noted Phentolamine (Rogitine) is the latest and seems to be reliable though both false negative and false positive results can occur *5 mg are injected intravenously or intramuscularly* and falls of systolic and diastolic pressures of 35 and 25 mm respectively are diagnostic

Treatment This is surgical Extreme fluctuations of blood pressure may occur during the procedure and may cause acute pulmonary oedema or even sudden death Intravenous infusions of rogitine to neutralize circulating hormone or of noradrenaline *to replace this if its sudden withdrawal leads to* collapse of blood pressure may have to be given and both should be ready

Steroid Hormone Therapy

In the last few years it has been shown that the adrenal glucocorticoids whether given themselves or released in large amounts on stimulation of the adrenal glands by ACTH are capable of profoundly modifying the symptoms and course of many diseases They seem to alter the responses of body cells to many external influences and to modify the characteristic changes of inflammation The swelling and pain associated with the latter are often greatly reduced yet paradoxically the resistance of the body as a whole to some forms of infection (notably tuberculosis) is lessened while natural healing processes may be retarded by an anti anabolic effect on the amino acids required for new tissue formation

These substances are not known to cure any disease in the sense that its cause is eliminated but they may so modify its course or reduce the severity *of the symptoms that the patient is better able to* overcome it or is tided over to a natural remission

Steroid hormone therapy carries a number of definite risks which must be clearly appreciated These risks are known and to a large extent complications can be prevented it is no more defensible to deny a patient a form of therapy that may be dramatically successful on account of vague misgivings about possible toxic effects than it is to *give these potent agents indiscriminately*

The adrenal glucocorticoids stimulate a poly*morphonuclear leucocytosis while causing eosino*penia and lymphopenia They produce euphoria and increase activity and appetite They raise the blood sugar level by opposing the action of insulin and by promoting gluconeogenesis from amino acids so producing a negative nitrogen balance They tend to cause sodium retention and potassium excretion by the kidney and may cause oedema and hypertension They modify the course of many infections and the processes of resistance to them as well as the normal responses of pain and inflammation *Adrenal androgens* which are derived from the breakdown of steroid hormones and also liberated during therapy with ACTH produce hirsutism seborrhoea and acne

Steroid hormone therapy may therefore produce leucocytosis fat deposition hypertension water and sodium retention oedema and potassium deficiency—a picture resembling Cushing s syndrome Rounding of the face hirsutism and obesity of the trunk may occur Glycosuria is common but diabetes very rarely persists after stopping therapy Infections may be lit up particularly tuberculosis Gastric ulceration may occur and perforation can take place almost silently Occasionally there are psychic disturbances with mania or depression

Steroid hormone therapy should therefore not be given to psychotics diabetics severe hypertensives and given only with great care to those with tuberculosis or with oedema During therapy a watch should be kept on the body weight the blood pressure the jugular venous pressure the lung bases the urine sugar and in longer therapeutic *courses on the chest X ray and blood* potassium The drugs should be given with caution where there has been peptic ulceration (though they may be very valuable in colitis when perforation is uncommon) A high protein low sodium diet is given with extra potassium chloride (3–12 g daily)

Several new steroid hormones prednisone prednisolone triamcinolone dexamethasone and methyl prednisolone have been shown to possess the anti inflammatory properties of cortisone with fewer side effects on electrolytes They are therefore *greatly to be preferred if there is any* tendency to oedema All these hormones if used in renal disease tend to raise the blood urea by promoting katabolism of amino acids

Principles of Therapy The aim should be to control symptoms as rapidly as possible and then to reduce the dose until the minimum effective level is reached This reduction should wherever possible be assisted by supplementary therapy with other effective agents in rheumatoid arthritis for example control can often be achieved with small doses of cortisone supplemented by aspirin or phenylbutazone All the adrenal steroids depress adrenal function they should therefore never be suddenly stopped or the patient may develop a

temporary Addisonian state This is particularly dangerous if the drugs are suddenly discontinued after an accident or in a surgical emergency so that there is a strong case for making every patient on long term therapy carry a warning card Moreover suddenly stopping therapy may cause a severe relapse or rebound of the condition being treated

Preparations Available ACTH Lyophilized powder Up to 40 units may be given intravenously in 24 hr by a saline drip or up to 200 units intramuscularly divided into 4 doses

Long acting preparation (gel) Given intramuscularly in one or two doses in the 24 hr up to a total of 200 units

Cortisone Acetate Tablets Given in 6-hourly doses of 12 5 to 100 mg orally

Suspension The same total dosage is given intramuscularly by one or two injections a day The slow absorption lasting several days leads to a much slower onset of activity than that of oral cortisone but a prolonged depot effect

Hydrocortisone (Cortisol) Similar to cortisone In addition there are preparations for intravenous infusion

Prednisone and Prednisolone are equivalent to about four times the same quantity of cortisone Given orally in 2 5 or 5 mg tablets In addition preparations are available for local use (including intra articular and conjunctival injection)

Methyl Prednisolone 4 mg tablets each equivalent to 5 mg prednisolone

Conditions Responding to Steroid Hormone Therapy Cortisone and its analogues constitute specific substitution therapy for panhypopituitarism adrenal deficiency and the adrenogenital syndrome The first of these can also be treated with injections of long acting ACTH at intervals of 24–72 hr

The diseases usually successfully controlled by cortisone and ACTH include acute rheumatism rheumatoid arthritis and spondylitis acute gout asthma and other allergic conditions pemphigus and exfoliative dermatitis giant cell arteritis regional enteritis and ulcerative colitis trichiniasis the active stage of sarcoidosis many inflammatory eye conditions many other types of collagen disease including disseminated lupus erythematosus periarteritis nodosa scleroderma and dermatomyositis the nephrotic syndrome acute toxic polyneuritis

This form of therapy may also be temporarily beneficial in acute leukaemia (apart from monocytic) multiple myeloma psoriasis and in some cases of infective hepatitis of pancreatitis and of thyroiditis

The Thyroid Gland

Development and Anatomy The gland develops from an entodermal bud early in the fourth week which arises from the pharynx at a point subsequently marked by the foramen caecum at the base of the tongue The bud grows caudally as a stalk (which is at first hollowed to form a duct) down as far as the thyroid cartilage when lateral growth occurs and the connexion with the tongue disappears The stalk may persist into adult life as the thyroglossal duct and aberrant thyroid tissue may be found in its course Anomalies of descent of the thyroid may lead to development of the gland anywhere between the base of the tongue and the posterior mediastinum

Normally the gland consists of two lateral lobes lying on each side of the larynx and trachea to which they are bound down by a sheath of deep fascia and connected by the isthmus which crosses the trachea just below the cricoid cartilage A small pyramidal lobe may project above the isthmus

Examination of the Gland The neck should be slightly extended and viewed both from the front and the side the patient should then be asked to swallow when the gland will be seen to move up with the larynx unless it is completely bound down to fixed structures by malignant infiltration or by adhesions associated with thyroiditis or previous surgery Engorgement of cervical veins may be seen when there is a goitre even when right auricular pressure is normal because the deep fascia may be under tension and may occlude them Any deviation of the trachea should be noted

The lateral lobes the isthmus and any pyramidal lobe present should be palpated in turn The lobes are more easily felt if the sternomastoid is relaxed on each side alternately by slightly turning the head to that side the larynx should also be pushed to that side with one hand and the lobe palpated with the other hand If the examiner stands behind the patient and presses one lobe back between the trachea and sternomastoid the other will be more easily palpable These manoeuvres should be repeated while the patient is swallowing

The normal gland may be palpable in a thin patient the right lobe being the more easily felt of the two

The consistency of the gland must be noted the overactive gland is usually firmer than normal A very hard gland may be the site of chronic thyroiditis or of cancer The gland may be tender in thyroiditis or after a haemorrhage into a nodule It is important to try to detect the presence of

nodules but small ones may be very difficult to feel The neck must also be examined for enlarged lymph nodes the one normally situated immediately above the isthmus must be distinguished from the pyramidal lobe

A bruit may be heard over a very active gland it must be distinguished from a murmur conducted from the underlying carotid artery

Retrosternal extension of a goitre may be noted when the patient swallows though it can often be diagnosed only by X rays which will also reveal any tracheal distortion Occasionally a goitre is entirely retrosternal or it may only become visible above the manubrium when the patient swallows (goitre plongeant)

Scanning the neck with a directional counter after a dose of ^{131}I gives important information about the activity of nodules and of particular areas in the gland

Synthesis of Thyroid Hormone The gland consists of masses of tightly packed follicles lined by polygonal cells In the resting state the follicles are filled with a clear colloid material and the lining cells are flattened when the gland is very active the colloid disappears and the cells become columnar forming papillary infoldings of the lining of the follicles

The cells concentrate iodide from the plasma and convert it to iodine which rapidly replaces hydrogen atoms in the benzene ring of the tyrosine nucleus forming di iodotyrosine Two molecules of the latter are oxidized by iodine and condense to form 1 thyroxine which is bound to protein and stored in the follicular colloid as thyroglobulin

The use of the radioactive isotope of iodine ^{131}I has greatly increased knowledge of the steps in this synthesis and of their control

1 *Iodide trapping* leads to a high concentration gradient for iodide between the gland and the plasma This gradient is higher in iodine deficiency and in hyperthyroidism and it is increased by thyrotropin It is also high when therapy with antithyroid drugs has depleted the body iodide Under all these conditions the rate of ^{131}I uptake by the gland is increased The trapping mechanism is inhibited by thiocyanate and by perchlorate and its efficiency is reduced by an increase in the available iodide

2 *Conversion of Iodide to Iodine and Organic Binding* is inhibited temporarily by antithyroid drugs such as thiouracil and carbimazole and by a rise in the concentration of iodine in the gland itself

3 *Discharge of Hormone from the Gland* TSH seems to promote the breakdown of thyroglobulin by a proteolytic enzyme thyroxine then diffuses into the bloodstream and circulates bound to a plasma albumin fraction (As iodide trapping is also increased by the action of TSH this hormone stimulates the activity of the gland) This step is inhibited by an increased concentration of iodide

It is evident that while control of thyroid function by the pituitary is by a feed back mechanism some autonomous regulation in accordance with the amount of iodide available also occurs In chronic iodide deficiency for example increased efficiency of the trapping mechanism may maintain a normal rate of hormone output if demands for the latter are increased as they may be at certain times such as puberty or if the diet contains antithyroid substances then the supply may be deficient when increased secretion of thyrotropin will stimulate the function of the gland and cause it to enlarge On the other hand an increased availability of iodide inhibits all phases of the gland s activity

The role of 3 5 3 1 triiodothyronine which has recently been isolated from the gland and is more active than 1 thyroxine in the treatment of hypothyroidism is uncertain It may be the form in which thyroxine exerts its ultimate effect on body cells

Investigation of Thyroid Function

There are three methods for estimating the rate of production of hormone by the thyroid gland in one an attempt is made to estimate it directly by measuring the rate of incorporation of iodine into the hormone in another the plasma concentration of the hormone is estimated and in the third the action of the hormone on body cells is measured

1 *Estimation of the Rate of Iodine Uptake by the Gland using ^{131}I* The assumption is made that the rate of uptake parallels the rate of hormone formation this is not true in states of iodine deficiency or after therapy with antithyroid drugs Three principal methods are available—

(i) The 2 hr and 24 hr ^{131}I uptakes are by far the simplest 10 μc of ^{131}I are given by mouth to the fasting subject and counts made over the gland with a directional scintillation counter The same quantity of the same solution of the isotope is placed in a test tube in a wax model of the neck and counts made over it immediately after this after subtraction of the background count

ing rate the ratio of counts (patient to phantom) × 100 gives the percentage uptake (decay being automatically corrected for) The normal ranges are 8–25 per cent at 2 hr and 10–50 per cent at 24 hr though every laboratory must derive its own range since the position and screening of the counter makes a slight difference The over active gland not only takes up more iodine than the normal but does so more quickly there is a growing tendency therefore to use the 2 hr uptake in diagnosis

(ii) *The neck thigh ratio* allows for the activity of tissues other than the thyroid itself Two hours after the dose has been given counts are made over the gland and over the thigh

(iii) *The estimation of the urinary excretion of* ^{131}I which varies inversely with the thyroidal uptake This has the advantage that only urine samples need be sent to the laboratory though collections must be complete A factor T is derived where

$$T = 100 \times \frac{(\% \text{ of dose excreted from 0–8 hr})}{(\% \text{ from 8–24 hr})\ (\% \text{ from 0–48})}$$

Normal values for T lie between 2 8 and 13

Whichever of the above methods is used for estimating the thyroidal uptake of ^{131}I the effect on the latter of abnormal iodide intake and of thyroiditis and of the administration of thyroid hormone both of which lower the uptake must be remembered A high uptake of ^{131}I due to iodide deficiency can be corrected by giving iodide for a week a low uptake due to recent administration of iodide can be detected by estimation of the urinary iodide Estimations of the protein bound iodine (PBI) in the plasma will give a normal value when ^{131}I uptake is low in thyroiditis but a high one when thyroid hormone has been taken

^{131}I uptake may be in the low normal range in pituitary myxoedema and may be high in cretins with goitres in these cases the BMR and PBI are abnormal

The advantage of ^{131}I uptake estimations is the fact that they are not affected by the patient s nervousness and they can easily be repeated after a week s administration of thyroxine (300 μg daily) which reduces the uptake of normal subjects to less than 20 per cent of the previous figure but has little effect in hyperthyroidism

2 *Estimation of the Protein bound Iodine in the Plasma* This is a tedious chemical analysis but if the butanol extractable fraction (BEI) is estimated (which eliminates circulating inorganic iodide) it gives a fair approximation to the level of circulating hormone The normal range is 4 0–8 0 μg/100 ml False low values are found for 24–48 hr after the administration of mercurial diuretics false high values occur after the use of organic iodine compounds for bronchography cholecystography or pyelography Lipiodol may remain in the bronchi for years and cause high BEI and PBI values Otherwise these are found only in infancy in pregnancy in hyperthyroidism and after the administration of thyroid hormone

The estimation of the protein bound ^{131}I 48 hr after giving 30 μc of the isotope by mouth is a much simpler procedure and avoids errors in the estimation of PBI due to organic iodine compounds A sample of plasma can be counted if it contains less than 0 2 per cent of the dose per litre the level of PBI is not raised

3 *Estimation of the Basal Metabolic Rate* This must be done by a competent person under standard conditions and should be done twice since unfamiliarity with the procedure and nervous tension always raise the estimation the first time

The BMR is the rate of heat production in the relaxed recumbent fasting patient In practice it is estimated from the rate of oxygen consumption and it can be assumed that after an ordinary diet the fasting R Q will be 0 82 when each litre of oxygen produces 4 825 calories The surface area is calculated from the patient s height and weight and the heat production is expressed in cals/m^2/hr The percentage by which it differs from the normal value for a patient of the same age and sex is calculated If the Robertson Reid scale of values is used the normal range is from +14 to −14 per cent

The BMR may be estimated after heavy sedation with barbiturates so that the patient sleeps during the test

High values may be found in nervous patients (in whom the tracing is often grossly irregular) after smoking and in leukaemia severe anaemia and cardiac and respiratory failure Incorrect values for surface area may be derived from the formula for this when the patient is very thin very fat or oedematous

4 *Estimation of the Blood Cholesterol* (normally 100–300 mg/100 ml) This may be useful as a check in suspected hypothyroidism or during its treatment but a value within normal limits may be abnormal for a particular patient Many factors besides thyroid activity affect it However the tendency of the level to rebound to a high figure within a few weeks of stopping thyroid therapy in cretinism makes this a valuable confirmatory test

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for a time The increased heat production causes cutaneous vasodilatation and sweating

The eyes are more often affected in younger patients There is an increase in the orbital fat causing protrusion of the eyeball and bulging of the lids Contraction of smooth muscle fibres in the levator palpebrae occurs and there is an increased amount of fat between the fibres of the ocular muscles *Exophthalmos* is common white sclera showing below the limbus when the patient looks straight forward though this may be masked by *periorbital swelling* *Lid retraction* due to spasm of the levator palpebrae often causes sclera to be visible above the limbus (Dalrymple s sign) There may be an associated over activity of the frontalis *Lid lag* detected by asking the patient to follow with the eyes an object moving downwards across the field of vision when an increased area of sclera is seen above the limbus is almost constantly present (von Graefe s sign)

The hands are nearly always warm and often moist and usually show a fine tremor of the ex tended fingers Cold wet hands with a coarse tremor are commonly found in neurotic patients and practically exclude the diagnosis of hyper thyroidism

The Cardiovascular System Evidence of a hyper kinetic circulation is found a rapid jerky often waterhammer type of pulse with a high pulse pressure (increased pulsation may be visible in the neck and in severe cases in the capillaries) and a diffuse apical impulse with a loud rough first sound and a systolic murmur The tachycardia per sists during sleep though it must be remembered that the normal sleeping pulse rate is below 70 and that some patients normally have a slower heart rate than this when up and about Congestive heart failure is common only in older patients when it does occur it is nearly always precipitated by an arrhythmia usually auricular fibrillation Occasion ally this is paroxysmal Older patients with toxic nodular goitre may have little other evidence of hyperthyroidism and the BMR and ^{131}I uptake may be within normal limits In such cases often termed *masked hyperthyroidism* it is probable that a very moderate constant increase in load has precipitated failure in a heart already abnormal

The Nervous System Tense restlessness in somnia excitability apprehension and depression are common These may be merely an exaggeration of the patient s previous personality traits which are often of a neurotic type A psychosis mania or delirium may occur The tendon reflexes are usually brisk

The muscles show a varying degree of atrophy Easy fatiguability is a very common complaint and widespread muscular weakness can be demonstrated in severe cases Spontaneous creatinuria is usual (a normal occurrence in children and women it is seldom found in normal men)

The skeleton may be affected in severe cases There is a tendency to a negative calcium balance though this may be corrected by a high intake while occasionally the blood alkaline phosphatase is raised and osteomalacia is seen in X rays of the bones In older women there is often evidence of osteoporosis in the spine and pelvis it is probable that since a negative nitrogen balance is common some diversion of amino acids from the bone matrix occurs and accentuates a tendency commonly pre sent after the menopause

The skin besides being warm and moist often shows areas of increased pigmentation and of vitiligo It is almost invariable to find at least some grey hair

Complications In addition to those mentioned above one or two complications are so striking that they form almost distinct syndromes

Exophthalmic Ophthalmoplegia may occur when the hyperthyroidism is not severe or even when thyroid function is normal It is much more com mon in men than in women There is oedema of the orbital contents with round-celled infiltration of the muscles There may be extreme exophthalmos with chemosis and corneal ulceration The first ocular movement to be affected is usually upward deviation later all may be involved

Thyrotoxic Myopathy While some muscular weakness and wasting is very common in hyper thyroidism occasionally the severity and distribu tion warrant the use of the term myopathy The pelvic and shoulder girdles are most affected Tendon reflexes are normal or reduced and the plantar responses are flexor There is no sensory loss The signs of hyperthyroidism may not be severe and muscular dystrophy motor neurone dis ease or dermatomyositis may be suspected

Myasthenia gravis and *periodic paralysis* may be associated with hyperthyroidism *Thyrotoxic crises* occasionally occur especially after thyroidectomy though they are now rare The onset is acute and the course fulminating with extreme restlessness prostration and mounting pulse rate and body tem perature Death may occur from hyperthermia or pulmonary oedema

Diagnosis. The diagnosis in the great majority of patients is made very readily Difficulty occurs chiefly in young neurotic patients and in older people with unexplained heart failure Even then laboratory investigations may be inconclusive it may be difficult for example to obtain an estimate of the metabolic rate under truly basal conditions

THYROID GLAND DISORDERS

Simple Goitre

It is probable that most non toxic goitres arise as a result of the cycle of alternating hyperplasia and involution that occurs in response to a waxing and waning stimulus to increased activity Hyper involution leads to the development of large colloid filled follicles lined by a flat epithelium forming a diffuse colloid goitre If this process is localized or irregular a nodular or adenomatous goitre may develop

Endemic goitre occurs in certain areas of the world (for instance Switzerland the Pacific North West and Great Lakes area of the U S A Derby shire and the South West of England) A large number of inhabitants may be affected though females are always in the majority Goitres may be *sporadic* In any area a goitre may be congenital

Iodine deficiency is undoubtedly the chief cause of endemic goitre which can be largely prevented by the use of iodized table salt No cause is usually apparent in sporadic cases though very occasionally goitrogenic substances may be responsible—brassica seeds turnips antithyroid drugs thiocyanates resorcinol (applied locally) and p amino salicylate

Clinical Picture The gland may be diffusely enlarged or especially in older patients a number of nodules may be palpable Even huge glands may cause very few symptoms Hyperthyroidism is not evident though a few patients develop this if iodine is given (Jod basedow ') A congenital goitre may cause difficulty in delivery or give rise to stridor asphyxia and dysphagia

Non toxic nodular goitre more commonly causes symptoms than colloid goitre The trachea may be compressed and angulated often causing dyspnoea on exertion or on lying down especially when there is an intrathoracic extension Rarely the entire gland is intrathoracic Haemorrhage may occur into the gland or into a cyst or nodule causing a sudden painful enlargement which may produce acute respiratory obstruction or dysphagia

Treatment Congenital goitres usually disappear within the first two weeks of life Iodine is valuable for the prevention and treatment of endemic goitre while sporadic diffuse goitres may respond to the administration of thyroid Surgery may be necessary if this fails or for complications Nodular goitres present a different problem for there is a definite risk of toxicity or of carcinoma developing and they should be removed (p 139)

Hyperthyroidism

Various names have been given to this condition the commonest being exophthalmic goitre thyrotoxicosis Graves s disease and Basedow s disease Secondary thyrotoxicosis Plummer s disease and toxic nodular or adenomatous goitre are synonymous The condition was recognized by Parry in 1825 Graves described the ocular complications in 1835 Rehn established the thyroid as the cause and performed the first thyroidectomy in 1884

Incidence and Aetiology The disease is much commoner in women than in men It is rare in childhood and commonest between 20 and 40 years of age There is a strong familial tendency Both endemic and sporadic goitres especially nodular ones may become toxic occasionally this seems to be precipitated by giving iodine There is uncertainty about the role of thyrotropin in the aetiology (p 118)

The onset is often related to emotional stress and may occur acutely after a shock Stress in animals has been shown to inhibit the release of thyroid hormone but to stimulate that of adrenal hormones it is possible that in this respect the patient who develops thyrotoxicosis reacts abnormally Many of these patients seem to be involved in difficulties which they are unable to solve

Clinical Picture In a typical case the diagnosis is immediately obvious The patient is often a thin young woman with prominent staring eyes and restless tremulous movements who complains of nervousness palpitation loss of weight in spite of increased appetite constant sweating and dislike of hot weather amenorrhoea and diarrhoea One or more of these complaints may dominate the picture and emotional or neurotic disturbances a change in the patient s personality extreme exophthalmos fatigue progressive loss of weight colitis or sterility may be the presenting symptom On the other hand even the patient with obviously severe hyperthyroidism may complain of remarkably little contrasting with the neurotic whose symptoms are out of all proportion to any physical signs that can be found In older patients symptoms referable to the cardiovascular system are much more common auricular fibrillation and congestive failure often dominating the clinical picture

The thyroid gland is almost invariably enlarged though the increase in its firmness may be more obvious than that in its size Occasionally the goitre is retrosternal A nodular goitre is common in older patients and may have been present for many years

Metabolism The BMR is raised and may be twice the normal the appetite is increased but loss of weight with negative balances of nitrogen calcium and phosphorus are usual Occasionally the appetite is so greatly increased that weight may be gained

more severe reactions including fever depression of leucopoiesis adenopathy and arthralgia occur in about 0 5 per cent All reactions are commoner in the first two months of therapy and with larger doses of the drugs with doses of carbimazole of less than 20 mg a day serious ones are almost un known Regular leucocyte counts are not a com plete safeguard against the most dangerous reaction agranulocytosis for the white count may fall early in therapy and rise again even when the drug is continued while agranulocytosis may develop quite suddenly The patient must be warned to report any reaction of any kind and if a sore throat occurs *to stop taking the drug immediately*

Methyl and propylthiouracil are given in doses of 200–450 mg/day carbimazole and methimazole from 15–45 mg/day according to the severity All these doses are divided by 3 and this amount given 8 hourly As soon as it is evident that the patient s symptoms are fully controlled and that weight and pulse rate are normal this must be reduced to a maintenance dose which may be 50–300 mg of the thiouracils or 5–20 mg of the other drugs The gland may enlarge soon after treatment is begun but get smaller again an increase in size later is usually a sign of overdosage

With careful observation a large number of patients respond well to therapy with antithyroid drugs and if these are discontinued after 18 months or 2 years the relapse rate is probably not more than 20 per cent A large number of the relapses occur soon after stopping the drugs Some patients however never seem to do well even with careful observation and dosage regulation It is doubtful whether there are many really resistant cases some patients are careless about taking the drug regu larly others dislike having to attend often in some an unsightly goitre develops a few develop toxic reactions It is probably wise to consider surgery as soon as it becomes evident that the course of medical treatment is not running smoothly

Thyroid crisis now rarely seen is a grave emer gency Absolute rest oxygen cold sponging for hyperthermia intravenous glucose and injections of vitamin B_1 should be *ordered It is usual to give* intravenous iodide (*e g* 1 gm sodium iodide 6 hourly) for its immediate antithyroid effect this in hibits the release of more hormone from the gland but cannot neutralize any already circulating 100 mg of hydrocortisone should also be given by intravenous infusion 6 hourly and antibiotics where there is infection Oral antithyroid therapy is begun immediately with heavy *sedation*

Exophthalmic ophthalmoplegia is the most de pressing of all the complications to treat The general principles are to control the hyperthyroid ism as carefully as possible without curbing it too abruptly or producing myxoedema (antithyroid drugs are therefore the safest therapy) and to pre serve sight The co operation of an ophthalmologist should be sought and tarsorrhaphy performed if corneal ulceration seems imminent With care and patience even very severe cases tend to recover slowly if their morale can be maintained If the condition is intolerable relief may follow Naff ziger s operation (removal of the orbital plates of the frontal bone to decompress the orbits) but even after this severe proptosis may continue Irradiation of the pituitary with small doses of X rays is some *times successful It is usual to give thyroid* by mouth to suppress thyrotropin secretion but it is rarely beneficial

Hypothyroidism

Thyroid deficiency occurring in the new born gives rise to *cretinism* Later in life thyroid failure results in *myxoedema* (qualified by the adjective *juvenile* when occurring in childhood or adoles cence)

In the absence of thyroid hormone normal growth and physical and mental development can not occur All functions are slowed There is an increase of intercellular mucoprotein throughout the body which involves particularly the muscles nerves and subcutaneous tissues

Cretinism was associated with absence of the thyroid by Curling in 1850 Gull described the nature of myxoedema in 1873 while the condition was very fully investigated by the Myxoedema Com mission of the Medical Society of London in 1888 Murray described the treatment by injections of thyroid extract in 1891

Cretinism

Cretinism occurs sporadically when the thyroid gland is usually absent or much more commonly in areas where goitre is endemic when both child and parents often have goitres

Clinical Picture The cretin is ugly and backward There is physical and mental sluggishness the skin *is dry cold grey and puffy The nose is flat* the lips and tongue large The muscles are flabby the abdomen is protuberant and there is often an umbilical hernia The child is constipated As it gets older it is obvious that development is retarded Growth is very slow and the body proportions re main infantile the limbs being short (p 121) Dentition is retarded X rays of the bones show *that the bone age is also retarded and the epiphyses* show in older cretins a stippling of the epiphyses which is characteristic Mental retardation is also severe the child usually being an idiot

and in toxic nodular goitre thyroid function tests may give results in the normal range Sometimes a period of observation in hospital makes the diag nosis apparent for the patient may have a raised sleeping pulse rate and may lose weight on a normal diet when no other cause for these abnormalities can be found It must be remembered that the eye signs may bear little relationship to the degree of thyroid over activity they may be absent in older patients with nodular goitres but very severe in younger ones with few other signs

The most helpful laboratory test is the estima tion of ^{131}I uptake care being taken to exclude other causes of an increase in rate and the test being repeated if necessary after a week s treatment with thyroxine (p 132)

If the diagnosis cannot be made with certainty a therapeutic trial with an antithyroid drug may be helpful Such a trial is especially justifiable in the older patient with cardiac failure and auricular fibrillation which has been found difficult to control with digitalis

Clinical Course Spontaneous remission is not un common in milder forms of the disease especially in young people Where weight can be maintained by an adequate diet and nervous symptoms largely controlled by sedatives it is reasonable to keep the patient under observation for a trial period without specific therapy especially if the eye signs are out of proportion to the degree of hyperthyroidism The exophthalmos of such patients may slowly im prove while surgical intervention or drastic anti thyroid therapy may particularly in males precipi tate ophthalmoplegia

On the other hand treatment may be a matter of urgency in older patients with congestive heart failure or when the condition has been overlooked or nutrition is poor and a crisis may occur

Treatment Three forms of therapy are now available sub total thyroidectomy antithyroid drugs and radio iodine No unanimity of opinion exists as to which is to be preferred and the special interests or skill of the physician or surgeon the facilities available and the local climate of opinion are usually the decisive factors

Subtotal thyroidectomy is now a very safe pro cedure the mortality under the best conditions being less than 1 per cent The patient should be prepared by a course of antithyroid drugs until thyroid function is nearly normal iodine is then given as well (Lugol s solution 1 ml daily for 10 days) to reduce the vascularity of the gland The two chief operative hazards are damage to the recurrent laryngeal nerves and removal of enough parathyroid tissue to cause postoperative tetany After 1 000 thyroidectomies Cattell reported hypothyroidism in 4 5 per cent tetany in 1 5 per cent recurrent laryn geal nerve injury in 1 0 per cent tracheotomy in 1 3 per cent recurrence in 2 4 per cent and mor tality 0 2 per cent

Surgery is especially valuable for the treatment of toxic nodular goitre and for the more severe forms of the disease in younger patients especially where eye signs are not extreme and the goitre is large In this group of patients there is however a small but definite relapse rate even after a very radical procedure and a second operation is rarely advisable Surgery is also better avoided when there is any evidence of ophthalmoplegia or where exo phthalmos is very severe especially in males for sudden changes in thyroid function may precipitate the fully developed condition

Radioiodine is coming into wider use in many clinics though it is usual to restrict it to patients over 40 years of age because of the theoretical risk of carcinogenesis The dose is between 1 and 8 mc of ^{131}I according to the estimated weight of the gland and may have to be repeated in 2 or 3 months The treatment is almost invariably successful thou h about 10 per cent of the patients may be expected to develop hypothyroidism This form of therapy is particularly valuable for patients who have relapsed after surgery and in older patients anxious to avoid operation

Antithyroid drugs are undoubtedly effective in controlling mild and moderately severe cases and in preparing the patients for operation They must however be taken absolutely regularly and at fre quent intervals for their effect is short lived Regular attendance and examination preferably by the same observer should be ensured for over treatment may lead not only to myxoedema but to considerable enlargement of the gland which may develop rapidly Some physicians combine anti thyroid drug therapy with regular doses of thyroid or thyroxine to suppress thyrotropin production in an attempt to prevent the occurrence of a goitre and the worsening of exophthalmos but it is doubt ful whether this is very effective

The drugs most commonly used are methyl thiouracil and carbimazole (Neomercazole) in Great Britain and propylthiouracil and methimazole (Tapazole) in the U S A Any of these drugs may cause a large number of toxic reactions though these appear to be fewest with carbimazole Drug eruptions particularly urticaria vomiting and diarrhoea headache dizziness and confusional states adenopathy arthritis jaundice drug fever neutropenia and agranulocytosis may occur Minor toxic reactions of which drug eruptions nausea headache and jaundice are the commonest occur in 1–2 per cent of patients treated with carbimazole

regained The dose should be gradually increased until the maximum clinical benefit is obtained and the laboratory tests are normal It is rarely necessary to give more than 200 mg (3 gr) a day

Juvenile Myxoedema

Thyroid deficiency may first occur at any time between birth and puberty when further growth and development will be lessened or will practically cease The longer it is left untreated the more difficult it is to restore the child to normal If it occurs before the age of 8 years some mental retardation will be permanent After this age treatment may be expected to restore mental function to normal though some skeletal retardation may persist puberty may occur at the normal age Such a patient has lost a certain period of normal physical growth which cannot be replaced The younger child however remains mentally backward as well Treatment by thyroid should be begun slowly and increased cautiously it is useless to try to force development for the result will be as psychologically disastrous as it is in cretinism

Thyroiditis

Acute thyroiditis may be suppurative or non suppurative Neither variety is common Pain occurs in the throat and is often referred to the sides of the face the ears and the back of the head The gland is swollen and tender Fever and rigors may occur The ^{131}I uptake ceases Suppurative thyroiditis must be treated with antibiotics and if necessary incision The non suppurative form which runs a less severe course terminates spontaneously though the symptoms can be rapidly controlled with cortisone

Chronic thyroiditis occurs in two forms known as Hashimoto s and Riedel s thyroiditis respectively

Hashimoto s thyroiditis (lymphadenoid goitre) occurs most commonly in adult females The gland is enlarged and infiltrated with lymphocytes The condition appears to be the result of auto immunity as circulating antibodies against thyroid extracts can be demonstrated

Clinical Picture The patient usually a middle aged woman complains of the symptoms of myxoedema or of the recent development of a goitre or of tenderness over the gland There may be a temporary phase of hyperthyroidism The gland is enlarged firm sometimes tender and is not attached to neighbouring structures Nodules are uncommon Besides the abnormal thyroid function there are often abnormalities in liver function tests (e g the thymol turbidity and colloidal gold) and certain specific tests are positive In the tanned red cell test the most sensitive red cells coated with thyroid extract are agglutinated by sera from patients with Hashimoto s disease These sera also contain antibodies precipitating human thyroglobulin as well as complement fixing antibodies

Thyroid extract should be given to control the myxoedema and in many cases the gland becomes smaller The goitre also disappears rapidly with deep X ray therapy but this increases the degree of myxoedema Surgery is unnecessary

Riedel's thyroiditis also occurs in middle age but in both sexes The gland is densely fibrous feels stony hard on examination and is found to be bound down to surrounding structures Hypothyroidism occurs The treatment is surgical

Carcinoma of the Thyroid

Carcinoma of the thyroid is a highly controversial subject There are many difficulties in assessing its true frequency and clinical course because it may occur in much younger subjects than most other forms of carcinoma because it may be of a very low order of malignancy often remaining almost stationary for many years and because of the difficulties of interpreting histological appearances (when those of the normal gland may vary so greatly according to its activity)

There is little doubt that carcinoma develops in a definite proportion of nodular goitres It may be very difficult to be certain however whether nodules are present in a goitre and if so how many there are Non toxic nodular goitre is a common disease but carcinoma of the thyroid is not. The only rational consequence of the knowledge that nodular goitre is precancerous is the total surgical removal of every nodular goitre which is impracticable Carcinoma is certainly commoner in single nodules than when the gland contains several but, often when a gland is removed because one nodule has been felt it is found that it contains many more It is wise however to remove all nodular goitres in young patients for it has been found that one third of single nodules under 15 years of age are malignant Any sudden enlargement or tenderness of a nodule (haemorrhage excluded) is suspicious With more extensive involvement, the gland becomes firm and irregular and may become bound down to other structures Fixation of a vocal cord from involvement of the recurrent laryngeal nerve is almost diagnostic Dysphagia may occur from infiltration not from pressure Occasionally the appearance of secondary deposits in the side of the neck in the chest or in bone may be the presenting sign The first is frequently mistaken for lateral aberrant thyroid tissue

Diagnosis It is imperative to make this as early as possible or some mental retardation will be permanent The appearance of Mongolian idiots is quite different they usually have a good colour and circulation and are lively and active In cretinism the ^{131}I uptake is low unless there is a goitre when it may be very high The blood cholesterol is nearly always raised and falls when thyroid is given if this is stopped it rapidly rises to even higher levels

Treatment Very young infants are given 15 mg ($\frac{1}{4}$ gr) of thyroid daily the dose being increased by this amount every month until the maximum benefit is obtained Development growth and skeletal maturation should then become normal The child should therefore be carefully weighed measured and X rayed at frequent intervals The blood cholesterol should be kept within normal limits The dose may have to be increased to 120 mg (2 gr) daily by 2 years and to 180 mg (3 gr) later Too large a dose causes excitement restlessness tachycardia and weight loss if the diagnosis has not been made until the child is older increasing the dose in an attempt to reverse the permanent damage merely turns a placid backward child into a restless nuisance

Myxoedema

Myxoedema is four times as common in women as in men it may arise at any age though it is most often seen in the middle years of life The onset is so insidious that the patient may not seek advice until it has been present for many years

Clinical Picture The symptoms that most commonly lead patients to seek advice are sensitiveness to cold cramps and paraesthesiae constipation or an alteration in the appearance the voice or the hearing Lethargy and apathy may be very marked and are more obvious to the relatives than to the patient A psychosis may develop with defects of memory and judgment depression delusions and hallucinations or the patient may lapse into coma Menstrual irregularities especially menorrhagia are common and sterility may occur from failure of ovulation

The face is puffy and pale though there is often a malar flush and a yellowish tinge from carotinaemia may be seen The hair is thin and brittle and tends to fall out from the head and eyebrows Speech is slow enlargement of the tongue causes some dysarthria and thickening of the vocal cords makes the voice deep and husky The patient may be overweight but severe obesity is uncommon the generalized deposition of myxomatous tissue however gives a swollen appearance though there is no pitting on pressure unless cardiac failure has caused oedema The skin feels dry and cold

The pulse rate is usually slow the heart may be enlarged and there may be evidence of congestive failure sometimes effusions into serous cavities occur The tendon reflexes show a characteristic abnormality relaxation being slow and prolonged this is particularly noticeable in the ankle jerk when the slow relaxation is obvious and diagnostic Deafness due to myxomatous infiltration of the acoustic nerve may occur

Diagnosis This is not usually difficult if the condition is thought of Laboratory tests usually show anaemia (normochromic or sometimes slightly macrocytic) often a high blood cholesterol a low uptake of ^{131}I and a low PBI and BMR The latter is particularly valuable in diagnosis and the result is usually below the normal range by the time the condition is suspected The ECG shows low voltage curves and flat T waves a chest X ray may show cardiac enlargement and the presence of a pericardial effusion The sedimentation rate may be raised and there may be albuminuria

Myxoedema may at first be mistaken for one of a number of other conditions including nephritis cerebral arteriosclerosis and simple anaemia but even after investigation there may be some doubt as to whether the condition is secondary to hypopituitarism To exclude this X rays of the skull and tests of adrenal cortical function may be necessary though the latter may be secondarily depressed in severe thyroid deficiency 17 ketosteroid excretion is usually subnormal for instance Even the failure of water diuresis that is so suggestive of adrenal deficiency may occur in severe myxoedema Sexual failure and amenorrhoea are suggestive of pituitary deficiency loss of weight strongly indicates this In pituitary deficiency the ^{131}I uptake and blood cholesterol may fall within the normal range

Treatment Treatment by dried thyroid by mouth produces a dramatic improvement It is wise always to start with a small dose *e g* 30 mg ($\frac{1}{2}$ gr) daily party because of the risk of precipitating an adrenal crisis if pituitary myxoedema has been overlooked but more particularly to avoid throwing too great a load on the abnormal heart which may precipitate angina auricular fibrillation or congestive failure There is never any point in giving thyroid more than once a day since each dose is not fully excreted for nearly 3 weeks The effect is therefore cumulative at first and by the end of 3 weeks treatment the patient is always very greatly improved If this is not obvious the diagnosis is doubtful At first there is usually a diuresis due to the removal of the abnormal intercellular myxomatous fluid so that a sharp loss of weight occurs Then the circulation improves the pulse rate rises the lethargy and paraesthesiae disappear and normal activity is

signs of a hypothalamic disturbance may be present such as sleepiness narcolepsy or thirst There may be signs of an intracranial lesion

Hypogonadism can be diagnosed only when the testes are unequivocally small or are shown to be atrophic by biopsy when the urinary FSH is increased or when eunuchoid proportions develop Cryptorchidism may suggest testicular deficiency The apparent size of the penis is no indication of the condition it is often concealed by fat

Treatment If there is no evidence of gonadal failure and it is felt that puberty is unduly delayed (it is reasonable to postpone therapy until 16 years) then chorionic gonadotropin should be given as for the treatment of eunuchism secondary to pituitary deficiency If this is ineffective substitution therapy with testosterone is required

Tumours of the Testis

The great majority of testicular tumours are malignant. Cryptorchidism was reported in 11 per cent of a series of 7 000 cases (the incidence in adult males is 0 23 per cent) Nearly all the patients excrete abnormal quantities of one or another hormone in the urine but there are usually no changes referable to their activities in the body

Seminoma occurs most often in the middle years of life The urinary excretion of FSH is often raised and does not fall after removal of the tumour that of oestrogen and of chorionic gonadotropin may also be increased and that of androgens diminished

Teratoma and chorionepithelioma may develop in childhood The excretion of oestrogen and of chorionic gonadotropin may be greatly increased there being enough of the latter to produce positive pregnancy tests in many cases of chorionepithelioma

Leydig cell tumours are very rare They occur at any age producing sexual precocity in children Gynaecomastia may occur in adults. The excretion of androgens is enormously increased the urinary 17 ketosteroids were reported to exceed 1 000 mg/24 hr in one case

The Ovary

Textbooks of gynaecology should be consulted for accounts of the functions and diseases of the ovaries The general effects of ovarian hormones and of their excess and deficiency are summarized below

Oestrogens stimulate the development of the female genitalia and breasts and the feminine characteristics They stimulate the action of osteoblasts and the fusion of the epiphyses the effect on growth is less than that of testosterone There is some protein anabolic effect and a tendency to produce the retention of sodium and water which may partly account for premenstrual water retention

Progesterone stimulates the secretory phase in an endometrium which has proliferated under the action of oestrogen and completes the development of the breasts It also has some salt and water retaining effect.

Ovarian Hypofunction

Oestrogen deficiency occurs after castration or the menopause after destruction of the ovaries by inflammation or tumour growth and with ovarian agenesis It may be secondary to pituitary failure and occur in chronic diseases just as testicular failure does and in these cases the urinary excretion of FSH is greatly diminished

Primary ovarian agenesis (*Turner s syndrome*) is a rare cause of stunted growth which may be mistaken for panhypopituitarism Many patients have been shown to be genetic males Sexual maturation never occurs the genitalia are hypoplastic and there is amenorrhoea There is usually a scanty growth of pubic and axillary hair Osteoporosis and delayed epiphysial union may occur though skeletal growth is greater than in most cases of dwarfism the patients often being about 4 ft 7 in tall, with eunuchoid proportions Certain congenital abnormalities are often associated the commonest being webbing of the neck and cubitus valgus Coarctation of the aorta may be present. The urinary excretion of FSH is greatly increased

Treatment. Many of these patients are content to remain untreated they may have no interest in the opposite sex and since they cannot have children prefer to remain unmarried Oestrogen therapy will stimulate sexual interest and by enlarging the vagina will make coitus possible the breasts and pubic hair may become normal little growth occurs but the skeleton matures and the increased activity of osteoblasts corrects the osteoporosis

Ovarian Tumours

These rarely produce endocrine changes though the following may do so—

Granulosa cell tumours which may occur at any age but are common after the menopause produce excessive amounts of oestrogen Sexual precocity occurs in children with periodic uterine bleeding and stimulation of growth and of the secondary

Neither hyper nor hypothyroidism is common with carcinoma Hot nodules are probably never malignant

The treatment is surgical Even the occurrence of distant metastases is not incompatible with prolonged life—*which makes any form of therapy very* difficult to assess in this disease Anaplastic lesions and many adenocarcinomas do not concentrate iodine so that ^{131}I can be used only in a proportion of cases

The Testis

The activity of the testis is stimulated by the *pituitary gonadotropins FSH acting on the seminiferous* tubules and ICSH stimulating the formation of testosterone by the interstitial cells

Testosterone is not a 17 ketosteroid and is not excreted in the urine However other androgens formed in the testis or derived from the metabolism of testosterone do contribute to the total urinary excretion of 17 ketosteroids Androgens stimulate the growth of the male accessory genitalia of the bones and muscles and of the pubic hair They *stimulate the activity of the osteoblasts* the formation of the osteoid matrix of bone the maturation of the skeleton and the retention of calcium and phosphorus They stimulate protein anabolism and hence nitrogen retention They bring about enlargement of the larynx and deepening of the voice and increased activity of sweat and sebaceous glands Haemopoiesis is also stimulated

Testicular Hypofunction

Testicular function is depressed in many chronic conditions particularly hepatic disease diabetes and severe malnutrition or it may be deficient as *the result of hypopituitarism in all these conditions* the urinary excretion of FSH is diminished In the Klinefelter syndrome (q v) there is a genetic defect Before puberty the testes may be absent aplastic or undescended they may be removed surgically or destroyed by trauma or inflammation at any age *In the great majority of these cases FSH excretion* is increased there is usually a failure both of spermatogenesis and of androgen production

Testicular failure occurring before the age of puberty gives rise to eunuchism Growth occurs for a longer time than normal and the skeletal proportions become eunuchoid (p 121) Muscular development is poor mild anaemia osteoporosis obesity and a feminine configuration are common facial hair is absent and the voice fails to break The external genitalia are small libido and potency are *absent* and gynaecomastia often develops When testicular failure is partial or occurs after puberty the abnormalities are less striking There may be some growth of facial hair so that the patient has to shave occasionally Erections may occur

Diagnosis It may not be apparent whether the *gonadal failure is primary or secondary to hypo*pituitarism An assay of the urine for FSH may clarify this but if no facilities exist for it a diagnostic trial with a course of chorionic gonadotropin (1 500 I U daily for 3 weeks) should be carried out. Enlargement of the genitalia indicates that secretion of androgen is occurring and therefore that the testes are responding to stimulation

The Klinefelter syndrome is a rare condition characterized by testicular atrophy azoospermia and gynaecomastia with increased urinary excretion of FSH The breast enlargement is not merely due to the deposition of fat there is an in*crease in the number of ducts and of* surrounding fibrous tissue Varying degrees of androgen deficiency occur and the skeletal proportions are eunuchoid There is strong evidence that some patients are genetic females and the condition appears to be the counterpart of Turner s syndrome

Treatment Eunuchism is treated by substitution therapy with androgens 5–10 mg of *testosterone* propionate in oil should be injected intramuscularly 3 times a week or 6 75 mg pellets implanted *every 3 months* Smaller doses may be effective in partial gonadal failure but where this is found to be secondary to hypopituitarism 1 500 I U of chorionic gonadotropin should be injected daily for a month this dosage is then halved for 2 months The course can be repeated after a 3 months interval

Delayed Puberty

There is a wide range of variation in the normal age for the onset of puberty the normal limits being arbitrarily considered to be 10 and 16 years Constitutional precocious puberty (p 127) may occur before this period however and be normal in every other respect *while delay until 18 or 20* does occur

The usual problem is that of the boy who shows no signs of puberty by the 15th or 16th year he may be rather obese and appear to have small genitalia

Frohlich s syndrome is a rare condition in which *obesity hypogonadism and often short stature* are associated with a lesion of the hypothalamus Other

plications of the former that chiefly menace them Their diabetes is essentially mild ketosis is unusual and carbohydrate tolerance is nearly always restored to normal by weight reduction

Mild diabetics are those in whom the hypergly caemia is usually easily controlled by moderate doses of insulin for which their requirements are usually fairly stable and in whom the metabolic disturbance is seldom severe enough to produce ketosis and coma

Severe diabetics suffer to a more marked degree from the disturbances of protein and fat metabolism that accompany insulin deficiency so that wasting and ketosis occur more readily They are usually unstable and are more difficult to control than mild cases Most children with diabetes are in this group

These divisions are arbitrary and should not be regarded as indicating the relative requirements for insulin The obese patient may in fact need very large doses of insulin to control the hyperglycaemia if the weight is not reduced while a much smaller dose than this may correct all the abnormalities of metabolism occurring in a severe case In all patients however infections and other forms of stress may increase the insulin requirements and form the first link in the chain of events leading to ketosis and coma

Complications These may be conveniently con sidered under the following systems—

Cardiovascular All forms of vascular degenera tion are common in diabetics but disease of the smaller branches of the arterial tree is particularly liable to occur Micro aneurysms of the retinal capillaries cause small punctate haemorrhages which are characteristic of diabetic retinopathy other punctate venous haemorrhages may be seen which ultimately form waxy exudates Hypertension is common so that the changes of hypertensive retinopathy may also be seen in the fundus Cataracts are common in older patients and may obscure these changes Disease of the coronary arteries may cause angina pectoris and myocardial infarction Gangrene of the extremities may occur not only from atheromatous occlusion of large vessels but from obstruction of smaller peripheral ones The renal and neurological complications of the disease may be largely the result of vascular degeneration

Respiratory Pulmonary tuberculosis is a common complication in younger diabetics and occurs in a more chronic form in older patients

Alimentary Fatty infiltration and enlargement of the liver is common especially in children Diar rhoea may occur and is sometimes troublesome at night

Genito urinary A particular form of vascular de generation occurs in the kidney—the intercapillary deposition of hyaline material in the glomeruli (Kimmelstiel Wilson glomerulo sclerosis) resulting in albuminuria and the nephrotic syndrome This is especially liable to occur in long standing mild diabetes and is commonly associated with retino pathy

Pyelonephritis is common in diabetes and one severe form—necrotizing papillitis with destruction of the renal papillae—though rare is particularly associated with it causing rapidly progressive renal failure Cystitis is common while fungus infections of the vulva in females cause severe pruritus In uncircumcised males infection and oedema of the foreskin (diabetic balanitis) may be severe and cause difficulty with micturition

The Nervous System A mild peripheral neuritis with loss of tendon reflexes and of vibration sense in the lower limbs is common (it must be remem bered that vibration sense is frequently reduced or absent in normal subjects after middle age) A more severe form may occur with numbness paraes thesiae severe pain and ataxia the calves are tender posterior column sense is lost and there may be peripheral loss of cutaneous sensation Inter stitial neuritis of peripheral nerves may also occur with foot drop sciatica or brachial neuritis Ocular palsies are not uncommon and the pupillary reflexes may be impaired A painless disorganization of a joint particularly of the feet may occur and resemble the Charcot joint of tabes Impotence and impaired sphincter control may develop in severe cases

Ketosis This is the most dangerous complication of the disease occurring when fat metabolism is so increased that peripheral utilization of acetone aceto acetic and β hydroxybutyric acids is incom plete these substances accumulating in the blood and being excreted in the urine There is a meta bolic acidosis with reduction of the blood bicarbon ate and loss of sodium and potassium in the urine (p 154) with severe dehydration ultimately produc ing circulatory failure respiration is stimulated but the effect is insufficient to correct the acidosis which together with the toxic effect of the abnormal meta bolites causes drowsiness stupor and then coma

Ketosis may be precipitated even in mild or obese diabetics by acute infections such as pneumonia boils or a carbuncle Anorexia usually occurs early and the patient may therefore omit his insulin Vomiting commonly follows increasing the degree of dehydration and from then on the progression is rapid

Diagnosis The diagnosis of diabetes mellitus is probable when the urine (which may be con veniently tested by using the Clinitest or Clinistix)

characteristics Ovulation does not occur since there is no formation of follicles In women either before or after the menopause irregular uterine bleeding occurs

Theca cell tumours are less common but may produce similar effects

Arrhenoblastomas arise from embryonic rest cells with masculine potentialities They are rare and develop in adult life producing virilism The urinary 17 ketosteroids may be increased

Leydig cell tumours are rare arising from cells of the ovarian hilus and producing virilism

Adrenal rest tumours may produce virilism or *Cushing s syndrome* sometimes with raised 17 ketosteroid excretion

Disgerminomas occur in young women They may produce sufficient chorionic gonadotropin for the urine to give a positive pregnancy test. There may be associated pseudohermaphroditism or mild virilization

Ovarian strumas are rare and it is possible that they arise from teratoma cells They may produce hyperthyroidism

Sclerocystic disease of the ovaries (Stein Levin thal syndrome) may be associated with amenorrhoea and mild virilization Hirsutism acne and hyper trophy of the clitoris are common and the 17 ketosteroid excretion may be slightly increased

Adrenal rest tumours are malignant the majority of the remainder are not

The Pancreas

The islets of Langerhans in the pancreas have the functions of an endocrine gland producing two hormones that control the metabolism of glucose—insulin secreted by the β cells and glucagon formed by α cells The production of both is prob ably stimulated by growth hormone (p 117) In sulin promotes the entry of glucose into body cells and the formation of glucose 6 phosphate under the influence of hexokinase thereby increasing the tissue utilization of glucose and promoting the storage of glycogen in liver and muscles It also *stimulates the entry of both protein and fatty acids* into the Krebs cycle Glucagon promotes hepatic glycogenolysis

Normally the level of glucose in the circulating blood is maintained within fairly close limits (80–120 mg/100 ml) as the result of a balance between its absorption and formation (gluconeogenesis) and its peripheral utilization the liver acting as a stabilizer which can take up glucose and store it as glycogen when absorption is more rapid than utilization and release it into the circulation again when the blood level is falling The actions of insulin are to some extent antagonized by growth hormone and the adrenal glucocorticoids the latter also pro moting gluconeogenesis from amino acids

When the production of insulin is insufficient hepatic glycogen storage is reduced so that the blood glucose level is allowed to rise above the normal upper limit when sugar is being absorbed while the reduced peripheral utilization retards the decline of this level The amount of *glucose filtered at the* glomeruli exceeds the reabsorptive capacity of the renal tubules *so that* glycosuria results and with it an osmotic type of diuresis leading to polyuria dehydration and thirst To provide calories in creased amounts of protein and fat are broken down leading to loss of weight muscle wasting and a negative nitrogen balance and to the in creased production of ketone bodies which may exceed the rate at which the tissues can utilize them causing ketosis

Diabetes Mellitus

Diabetes mellitus is characterized by the disturb ances of metabolism which result from a relative or absolute deficiency of insulin Von Mering and Minkowski showed that diabetes followed the re *moval of the pancreas in 1889 Banting* and Best isolated insulin from the pancreas in 1921

The disease seems to be transmitted as a men delian recessive characteristic theoretically if two diabetics marry all their children will ultimately develop the disease if they survive long enough If a diabetic marries into a non diabetic family none of the children will develop the disease but some may be carriers and may have diabetic children if they marry diabetics or other *carriers In prac* tice however this seems to be an over simplifica tion for other factors such as obesity chronic in fection and endocrine disorders play a part in determining the onset of the disease

Clinical Picture The onset of the disease may be acute with thirst polyuria rapid loss of weight and even coma often occurring during an infection or some other form of stress or it may develop in sidiously *especially in older patients*

Three main types of patient are readily recogniz *able the obese the mild and the severe*

Obese diabetics are disturbed mainly by symp toms referable to the glycosuria—thirst polyuria and in women pruritus vulvae It would otherwise be more correct to regard them as sufferers from obesity rather than from diabetes for it is the com

quire insulin They are seldom overweight protein and fat catabolism are increased and ketosis and coma readily occur It is sensible to give such patients a diet sheet (*see* below) with a fair number of alter natives partly to make sure that the calorie intake is adequate but also because many patients pick up queer ideas about a diabetic s food requirements from gossip or the newspapers Many are convinced that provided they never touch sugar all will be well

Fifteen calories should be allowed per lb of ideal weight for moderately active men 10–20 per cent more may be given for manual work Women doing housework may be given 10 per cent less In every patient however the diet should be adjusted to maintain the ideal weight when hyperglycaemia is controlled

At first the patient may have to weigh the por tions of food but this very soon becomes unneces sary

One gramme of protein should be allowed for every 2 lb of body weight 40 per cent of the calories may be given as carbohydrate About 100 g of fat will be required for the average adult This amount should be reduced if the blood cholesterol is high or if there is arterial disease

	Carbo hydrate	*Protein*	*Fat*	*Cal*
Breakfast				
Cereal 1 cupful (1 oz)	20	2	0	88
1 egg or 1 small por tion of fish (1 oz)	0	7	5	73
Lunch and Dinner				
Medium portion (2 oz) of meat or fish or two slices of cold meat	0	14	10	146
Two small potatoes	20	2	0	88
Green vegetables or salad Medium sized apple (4 oz) or banana small grapefruit or orange	10	0	0	40
Divide as required be tween the three main meals and three small ones—				
Milk one pint	28	20	20	370
Bread three thin slices (3 oz)	45	6	0	204
Butter (1 oz)	0	0	30	270
6 plain biscuits	30	3	6	180

The diet should contain three main meals with snacks in mid morning mid afternoon and before retiring The basic diet above provides 1 750 cal with 180 g of carbohydrate

More calories can be provided by increasing the portions and by the following extras—

1 teaspoonful of sugar jam marmalade or honey or
1 Vita Weat biscuit providing 5 g of carbo hydrate
1 oz of chocolate (non diabetic) 120 cal (30 g carbohydrate)
1 medium rasher of bacon 60 cal
1 oz of ice cream 60 cal (6 g carbohydrate)
1 oz of cheddar cheese 120 cal (7 g protein)

Insulin should be given in such doses that all disturbances in metabolism are controlled weight is gained and in children normal growth is restored It is not essential or even possible to avoid completely the occurrence of hyperglycaemia or even glycosuria though the absence of these pro vides a convenient index of the adequacy of insulin replacement Such complications as blindness gangrene and renal failure chiefly occur in the old the main causative factor being the duration of the disease for they rarely occur until it has been present for more than 10 years Long term studies however suggest that their incidence is reduced by careful control of the hyperglycaemia throughout the course of the disease This does not imply how ever that frequent blood sugar estimations are required in every case Once it is known that the patient is stable and is intelligent and co operative and that the renal threshold for sugar is normal it is probably wiser to rely on regular urine testing rather than on occasional blood estimations for maintaining control

Choice of Insulin Soluble (or *regular*) *insulin begins to lower the level of the blood sugar within* a few minutes of its injection subcutaneously its action is maximal in about 2 hr and then declines over the next 6 hr *Insulin zinc suspension (semi lente)* has a similar effect *Globin insulin* has a maximum effect lasting from 4–12 hr after in jection *Insulin zinc suspension (lente)* and *Isophane (NPH) insulin* have maximum effects lasting from 6–18 hr while those of *Protamine zinc insulin (PZI)* and *insulin zinc suspension (ultra lente)* are greatest from 8–24 hr

Soluble insulin should be used whenever a rapid effect is required when ketosis has to be corrected or insulin has to be given intravenously It may be necessary to inject it 2 or 3 times a day in very un stable cases or when preparing the patient for surgery or for labour or in children Globin insulin is suitable for mild or moderate cases particularly when a very large meal is eaten at mid day since

is found to contain a substance reducing Benedict's solution Some reduction may occur when the urine *contains lactose* which is excreted by lactating women homogentisic acid pentose laevulose or a large amount of glycuronates Glucose can be identified by the use of Clinistix

Glycosuria may occur when the blood sugar level *is less than 180* mg/*100* ml if the renal tubular reabsorption of glucose from the glomerular filtrate is low (*renal glycosuria*) which may occur in some pregnant women or as an isolated benign abnormality or as part of the Fanconi syndrome Otherwise glycosuria indicates hyperglycaemia the blood level being above 180 mg/100 ml

A more precise indication of reduced carbohydrate tolerance is given by the level of the blood sugar 2 hr after the ingestion of 50 gm of glucose (In America it is usual to give 100 gm which makes little difference to the 2 hr level though it further prolongs the abnormally high level in diabetes) This level should not exceed 130 mg/100 ml using the Folin Wu method on venous blood If a method is used which estimates true glucose (such as that of Harding) the figure should not exceed 110 mg Capillary blood is more variable owing to the variable arterio venous difference

Hyperglycaemia may occur transiently in emotion after a large carbohydrate meal in hyperthyroidism when feeding is resumed after starvation in infections and in head injuries meningitis and cerebral vascular accidents It may occur with an adrenal phaeochromocytoma With these exceptions *it indicates diabetes mellitus In all except* mild cases of this condition there is also fasting hyperglycaemia It is rarely necessary except when investigating the renal threshold to carry out the full glucose tolerance test in which the blood sugar *is estimated every* $\frac{1}{2}$ *hr for* $2\frac{1}{2}$ *hr after the ingestion* of 50 gm of glucose

Diabetic ketosis should be suspected whenever a diabetic patient complains of drowsiness nausea vomiting unusual constipation or abdominal pain particularly if there is evidence of infection recent trauma or laxness in the use of insulin In comatose patients the odour of acetone in the breath the obvious dehydration and *Kussmaul breathing* will suggest the diagnosis which will be confirmed by the finding of acetone in the urine or plasma (both can be readily tested by the Acetest adaptation of Rothera's test) Comatose patients suffering from *meningitis* cerebral vascular accidents or the effects of head injury may be found to have glycosuria but acetone will be present only if metabolism has been disordered by a prolonged *period of starvation* or dehydration

Since Rothera's test can now be so easily carried out by the patient using the Acetest there is a strong case for supplying all but the mildest, most stable diabetics with these tablets and telling them to test the urine whenever they have an infection feel off colour *or lose their appetites They should* report at once to the doctor or clinic if it is positive Diabetic coma which has already become uncommon with the increased understanding of the disease would be largely prevented if this were done *In the clinic the finding of a positive* Rothera's test should be followed by testing the urine with ferric chloride solution which is added drop by drop (Gerhard's test) A Bordeaux red colour developing after the phosphates have been *precipitated indicates a degree of ketosis* calling for urgent in patient treatment (Salicylates excreted after tablets containing aspirin have been taken give a positive test which persists when this is carried out after vigorously boiling the urine acetone being volatile is driven off by this and the colour does not then develop)

Treatment This will depend upon the type of case and the presence or absence of complications particularly ketosis

In the obese the most important therapeutic measure is weight reduction (p 158) The limits of the patient's ideal weight should be written conspicuously in the notes and even *an excess of a* few pounds corrected The glycosuria and the associated thirst and the pruritus vulvae that is so often the presenting symptom in obese women frequently disappear dramatically with the loss of only *a few pounds* and this should be emphasized to encourage the patient to persist until a normal weight is attained when the fasting and 2 hr blood sugar levels usually return to the normal range There is little risk of ketosis occurring during this *process* provided there is no infection and it is a tactical error to prescribe insulin before the weight is reduced for appetite is stimulated and progress may then be impossible

Infection should also be vigorously treated when impaired carbohydrate tolerance may improve

Mild diabetics who are not over weight and who develop hyperglycaemia and glycosuria after large *carbohydrate* loads may not do so if the carbohydrate in the diet is moderately restricted and more evenly distributed In other mild cases it may be possible to prevent *hyperglycaemia by the oral* administration of chlorpropamide (Diabinese) 250–500 mg every morning which seems to reduce the hepatic output of glucose It is not a true insulin substitute and no attempt should be made to control *hyperglycaemia* by its use except in mild diabetes of recent onset

More severe cases and practically all children re

2 Blood should be taken for the estimation of sugar bicarbonate sodium potassium and chloride 50 units of soluble insulin are injected intravenously by the same needle

3 An intravenous infusion of sodium chloride and lactate is given If there is evidence of shock and low blood volume the latter should be rapidly restored with blood plasma dextran or albumin before starting this infusion

4 50 units of soluble insulin are given sub cutaneously with 1 megaunit of penicillin i m

5 The bladder is catheterized and the urine examined for sugar and ketones every hour

6 A tube is passed into the stomach which is washed out with 5 per cent sodium bicarbonate

7 When the blood estimations are available the intravenous infusion is modified by adding more sodium lactate or potassium chloride to correct acidosis and potassium deficiency (p 155) It should be made up on a basis of 5 per cent glucose

8 50 units of insulin are given subcutaneously every hour until the glycosuria and ketonuria are diminishing and then reduced to 4 hourly injec tions of 25–50 units according to the glycosuria Severely ill patients whose usual insulin dose is high may be given an initial dose of 200–400 units

9 As soon as the patient can swallow sweet ened fruit drinks and tea are given by mouth

10 The blood estimations are repeated in 6 hr and the composition of the infusion modified accordingly

11 As the ketosis disappears the change over to oral feeding at frequent intervals with ample fluids is made gradually the infusion being dis- continued

Diabetes and Surgery Only life saving procedures should be carried out in diabetics without a pre liminary period of preparation in hospital If an immediate operation is essential and as is often the case ketosis is present the blood sugar and bicarbonate should be estimated and the patient sent to the theatre with an intravenous infusion of 10 per cent glucose and ¹ molar sodium lactate run ning at 2 ml/minute 50 units of insulin are given intravenously if the patient is in coma otherwise 50 units may be added to each 500 ml of infusion and so given over 4 hr Insulin is also given sub cutaneously on the above lines

In all other cases a short period of hospital observation and management is advisable before operation The daily dose of insulin should be divided into four injections of soluble insulin the first being given subcutaneously with a glucose drink not less than 3 hr before the operation un less the anaesthetist forbids it In that case and wherever the procedure is a prolonged one an in travenous infusion of 10 per cent glucose should be started at 2 ml/minute the soluble insulin being given every 6 hr As soon as the patient can pass urine it is tested for glucose and acetone and the further doses of insulin modified accordingly

Diabetes and Pregnancy Carbohydrate tolerance often decreases during pregnancy especially in the last three months Insulin is nearly always required to control this and the degree of control should be as exact as possible As the infant is often larger than normal and there is a high rate of still births labour should be induced at 36 weeks (many prefer to perform caesarean section) The patient should first be changed over to soluble insulin and during labour this should be given in divided doses 6 hourly with ample glucose drinks The infant should be watched carefully for hypoglycaemia due to hyperplasia of the islets of Langerhans

Hypoglycaemia

The blood sugar level may fall below the normal lower limit under the following circumstances—

1 In Addison s disease when liver glycogen storage is deficient in the absence of glucocorti coids

2 In panhypopituitarism when there is the additional deficiency of growth hormone In both these conditions hypoglycaemia occurs readily on fasting and may cause coma

3 In hepatic insufficiency and glycogen storage disease

4 In the presence of excess circulating insulin either exogenous or endogenous the latter being produced by a tumour of the islets of Langerhans

5 In pregnancy and lactation and at certain times in otherwise normal persons particularly after severe exercise (functional hypo glycaemia)

Symptoms tend to occur when the blood sugar level has fallen below 60 mg/100 ml At first there are sensations of hunger and of impending collapse followed by the release of adrenaline with pallor trembling sweating and palpitation confusion or even mania may occur and there may be hyper reflexia extensor plantar responses and focal or generalized convulsions Recovery is usually spon taneous though in all except functional cases the hypoglycaemia may be prolonged responding only to the ingestion of food or the injection of glucose and occasionally ending fatally After prolonged hypoglycaemia permanent focal signs in the nervous system such as a hemiplegia may remain

Functional hypoglycaemia is particularly liable to

the morning dose exerts its maximum effect during the afternoon The great majority of diabetics can be controlled by injections once a day of soluble and protamine zinc insulins or of mixtures of the insulin zinc suspensions The advantages of the latter are their purity (so that sensitivity reactions are avoided) the ease with which lente insulin (a mixture of 3 parts of semi lente with 7 of ultra lente) can be modified by adding more of one of its constituents to suit the individual patient and the fact that these can be mixed in the syringe without thereby changing the dose of each constituent (as occurs when S I and P Z I are mixed since the latter binds some of the former)

Once the decision has been taken to treat the patient with insulin he should be given a diet sheet and instructed in urine testing self injection and the importance of weight regulation of the avoidance of ketosis and of the dangers of hypoglycaemia If there is no ketosis and if there are no complications such as infections or severe malnutrition that make continual observation advisable insulin therapy can be begun and supervised in the Out Patient Department It is often said that patients must be admitted for stabilization but in fact the resumption of full activity after rest in the Ward always requires the reduction of the dosage of insulin and sometimes precipitates hypoglycaemia so that the object of stabilization is often defeated

Once the patient has been given a satisfactory diet sheet and understands how to inject insulin and to look after his syringe therapy can be begun with a small dose of I Z S lente (6 or 8 units half an hour before breakfast) The urine should be tested 4 times a day the bladder being emptied on rising and before lunch dinner and retirement The dosage should be gradually increased until the majority of the specimens are blue on testing an occasional green being advisable to avoid hypoglycaemia If mid day glycosuria persists more semi lente should be given if there is only early morning glycosuria additional ultra lente is required If the patient wakes with headache hypoglycaemia has occurred during sleep and the total dose of lente should be reduced but more semi lente given In some patients the disease can apparently be more easily controlled with the use of S I and P Z I in America it is usual to use either the latter mixture or N P H insulin with or without regular or crystalline insulin

Every diabetic should know the importance of the care of the feet which should be kept warm dry and clean with well fitting shoes and the frequent use of a fungicidal powder The routine of attendance at a diabetic clinic with regular weighing and medical examinations and frequent chest X rays besides the opportunity afforded to compare progress with other patients is very valuable

Hypoglycaemia is particularly liable to occur if the patient fails to eat within half an hour of the injection of insulin or if unusual exercise increases the utilization of glucose Weakness hunger headache sweating and a feeling of impending collapse may rapidly give way to confusion coma and convulsions if sugar is not taken at once The patient should carry sugar and a warning card If the patient is first seen when in coma the time and rapidity of its onset and the absence of dehydration of evidence of infection and of ketones in a specimen of urine (obtained if necessary by catheter) rule out diabetic coma 0 5 ml of adrenaline 1 in 1 000 should be given subcutaneously and 50 ml of 50 per cent glucose intravenously If neither is available sugar may be given in solution rectally It should be remembered that morning headache is the usual sign of nocturnal hypoglycaemia caused by long acting insulins

Diabetic Ketosis The discovery of a moderately positive Rothera s test on the urine with a negative Gerhard s test calls for increased vigilance a search for infection and more insulin If infection is found the dosage of insulin may have to be increased considerably and extra carbohydrate given (If as is often the case there is anorexia liberal glucose drinks are prescribed) Even mild and obese diabetics may need very large doses of insulin in the presence of infection though it may often be discontinued once recovery has occurred

A strongly positive Rothera s test on the urine or plasma with a positive Gerhard s test is an indication for immediate hospitalization and 6 hourly injections of soluble insulin together with vigorous treatment of any infection The diet should be divided into four meals with ample carbohydrate and given to cover the insulin each dose of the latter being one quarter of the patient s usual dose together with an increment depending on the amount of sugar in the immediately preceding specimen of urine In this way the total amount given in 24 hr may be double the usual dose or even more If the patient has not previously had insulin the first dose can be one of 20 units succeeding ones being increased or decreased according to the glycosuria

If the patient is admitted in a severely stuporous state or in coma management must be planned along the following lines—

1 An immediate examination must be made to assess roughly the degree of dehydration (p 155) and the role of infection

(codfish vertebrae) and the nucleus pulposus may herniate through the end plates producing Schmorl s nodes in the radiographs Individual vertebrae may be wedged or collapsed

Osteoporosis is commonly confined to the spine and pelvis but the other two conditions are more widespread The resorption of bone in *osteitis fibrosa* is seen particularly in X rays of the hands where the thin layer of cortical bone of the pha langes is seen to be absorbed in a lace like manner and of the skull which has a ground glass appear ance The lamina dura round the roots of the teeth normally present except in the edentulous is absorbed (the teeth themselves are unaffected) Cysts of bone and solid tumours composed of osteoblasts and osteoclasts which resemble cysts in the X rays are both seen especially in the cortex Bending of the long bones and deformities of the pelvis occur and fractures are common In *osteo malacia* there is a uniform decalcification the skull may appear mottled and rarely the lamina dura be absorbed but subperiosteal resorption is not seen Ribbon like areas of decalcification (Looser s nodes or pseudo fractures) may be seen in the bones often symmetrically Bending is more common than frac ture *Rickets* represents a particular form of osteo malacia in which preparation for growth is excessive but imperfect with irregularity and faulty calcifica tion of the provisional zone in the epiphysial plate

Osteoporosis

O teoporosis occurs when the osteoid matrix of bone is deficient as in scurvy (since vitamin C is necessary for the formation of the collagen) mal nutrition and thyrotoxicosis (when there is a nega tive nitrogen balance) and in Cushing s syndrome (when protein deficiency occurs from diversion of essential amino acids to gluconeogenesis) It occurs in gonadal deficiency and after the menopause since sex hormones stimulate osteoblastic activity It also occurs in disuse atrophy following immobilization or poliomyelitis in acromegaly and in senility Occasionally idiopathic cases are seen none of the above causes being found The vertebrae and pelvis are most often affected (except in disuse atrophy of a limb) The plasma calcium is normal except when the condition occurs rapidly after im mobilization when a rise may occur and be associated with hypercalciuria The plasma phos phorus may be in the higher normal range the alkaline phosphatase is normal which reflects a failure of the osteoblasts to respond to the increased skeletal strains

Symptoms In acute cases hypercalciuria may be sufficient for a renal calculus to form There may be a sufficient rise in the plasma calcium level to confuse the diagnosis Pain and deformity are common when vertebral osteoporosis is severe and compression fractures may cause root pains and paraplegia Spontaneous fractures in long bones are common in senile cases

Treatment Immobilization must be avoided whenever possible Even when there are fractures of vertebrae it is best for the patient to be up and about with a spinal support A high protein diet and sex hormone therapy are often beneficial Testosterone is the most effective causing nitrogen phosphorus and calcium retention 20 mg can be given daily sublingually or an implant of 200 mg subcutaneously every 3 months

Osteomalacia

Osteomalacia or failure of calcification of the osteoid matrix occurs from deficient intake or absorption of vitamin D or in resistance to its action It may occur in many forms of renal disease and in certain cases with increased urinary calcium loss

Either the plasma calcium or the phosphorus is low so that their product is subnormal osteoblastic activity is increased with a rise in plasma alkaline phosphatase In many cases parathyroid hyperplasia occurs and maintains the plasma calcium level at a normal or near normal figure It is doubtful whether this activity is ever sufficient to raise the level above normal unless true adenoma formation has occurred

Deficiency of vitamin D is now rare in Western countries though it occurs in Northern China In children under two years of age it causes rickets (p 161) In X rays of the metaphyses the widened rachitic intermediate zone of defective calcifica tion is seen where bending occurs Irregularity of the epiphysial plate with cupping of the metaphysis and fraying of the end of the shaft of the bone is seen

Resistance to vitamin D is a rare condition in which rickets persists into adult life very large doses of the vitamin may be needed to correct it

Impaired absorption of vitamin D occurs in steatorrhoea (coeliac rickets) or after removal of a large part of the small intestine Mild degrees of steatorrhoea are often overlooked as diarrhoea may not occur In *renal disease* osteomalacia may occur in chronic renal failure with azotaemia in associa tion with osteitis fibrosa (The latter is often said to be caused by the acidosis but there is very little evidence for this and parathyroid hyperplasia occurs p 150) The osteomalacia itself responds to large doses of vitamin D In certain renal tubular

occur in neurotic patients the episodes being brief but frequent They may be precipitated by large carbohydrate meals and a prolonged glucose tolerance test may demonstrate hypoglycaemia after 3 or 4 hr

Tumours of the islets of Langerhans are usually adenomas but about 20 per cent are carcinomas The increased secretion of insulin causes severe and often prolonged attacks of hypoglycaemia the blood sugar falling below 40 mg/100 ml The treatment is surgical and the outcome is often favourable even when the tumour is malignant.

Metabolic Bone Disease

Calcium and Phosphorus Metabolism These elements are mainly derived from dairy products in the diet though in Great Britain flour is fortified with calcium The absorption of calcium and phosphate is increased by vitamin D which is fat soluble Part of the intake is always lost in the faeces but calcium is also excreted in the bowel so that a negative balance occurs on a very low intake

Normal plasma levels are 9 0–10 5 and 3–4 mg/100 ml for calcium and phosphorus respectively though the latter may be 5 in growing children (The product of these values lies between 30 and 40 in adults and between 40 and 55 during growth) The calcium in plasma is present partly in an ionized form partly in combination with plasma protein and partly complexed with organic acids

The urinary excretions of both calcium and phosphorus are closely linked to the filtration rate Calcium disappears from the urine at plasma levels below 7 0 mg/100 ml and increases as the level rises Mixing the urine with an equal volume of the Sulkowitch reagent (ammonium oxalate + oxalic acid) gives an indication of the amount of calcium present there being enough normally to produce a milky appearance Whatever the dietary intake the 24 hr excretion rarely exceeds 200 mg The plasma phosphate rises as the filtration rate falls in progressive renal disease and this in turn depresses the plasma calcium level Vitamin D tends to depress phosphate reabsorption by the tubules parathormone does this to a much greater extent This hormone therefore tends to lower the plasma phosphate and so to raise the level of ionized calcium it also has a direct action on the bones but this is less well understood

Normal Bone Formation Bone may be formed in one of three ways *Endochondral* formation accounts for most of the skeleton apart from the clavicle and the vault of the skull Cartilage cells in growing bone proliferate in rows the substance between them calcifying Blood vessels break into this so that osteoblasts can lay down osteoid matrix on the cartilaginous surface These cells secrete an enzyme (alkaline phosphatase) which apparently hydrolyses inorganic phosphorus compounds and by increasing the local concentration of phosphate causes the deposition of a calcium carbonate-phosphate complex on the osteoid seams

At the same time multinucleated cells—the osteoclasts—are engaged in resorbing the seams of bone elsewhere and the bone laid down directly to replace them is termed *endosteal bone* In this way bone is remodelled constantly throughout life and its structure can be modified to meet particular stresses *Membranous* bone is formed directly in specialized mesenchyme or under the periosteum

Metabolic Bone Disorders

Three conditions occur in which there is a generalized tendency to loss of strength and of radiological density of the bones Each has a characteristic histological appearance while there are certain differences that often enable a distinction to be made between them in X rays It must be remembered however that reduction of bone density is not apparent in an X ray until a very considerable loss of bone has occurred and even then can be detected with certainty only by comparison with the X ray of the same bone in a normal subject taken under identical conditions (preferably on the same film)

In *osteitis fibrosa* bone resorption exceeds the rate of endosteal bone formation though the latter is stimulated by the increased strains incurred by the weakened bone This increase is reflected in a raised plasma level of alkaline phosphatase (normally 3–5 Bodansky or 3–13 King Armstrong units per 100 ml in adults and up to twice this level in growing children)

In *osteoporosis* there is a deficiency of osteoid matrix The alkaline phosphatase is not raised since endosteal bone formation is not increased In *osteomalacia* there is deficient calcification of the osteoid matrix alkaline phosphatase is high

All three conditions particularly affect the vertebral column the vertebrae become biconcave

patients with vague bone pain and tenderness and with renal calculus The Sulkowitch reagent test is helpful a very heavy turbidity is always suggestive Estimation of the 24-hr urinary calcium excretion may show that this exceeds 200 mg—this is unusual whatever the intake If it persists on a 3-day low calcium intake (the diet should consist of fruit lean meat, potatoes tea and coffee with sugar but no milk, bread or rolls of known low calcium com position and preserves) the diagnosis is almost certain The normal plasma calcium level is not above 10 6 mg/100 ml levels higher than this are always suggestive especially if the phosphorus is low though renal failure may reverse this Where the calcium level is in the upper normal range de termination of the ionized calcium level is neces sary this is always raised whatever the total calcium level

Treatment Surgical exploration of the neck (and of the mediastinum if no abnormal parathyroid tissue is found there) and removal of the adenoma or of nearly all the hyperplastic glandular tissue

Hypercalcaemia

Hypercalcaemia occurring with hyperparathyroid ism is usually accompanied by hypophosphataemia If urinary calculus formation has led to renal failure the blood phosphorus may be raised when the high calcium level may be depressed

Hyperparathyroidism may occur secondarily to chronic renal failure with raised blood phosphate it tends to raise the blood calcium though this rarely exceeds the normal level Metastatic calcifica tion may then occur the deposition of calcium salts round joints particularly the shoulder joints is much commoner in this secondary hyperpara thyroidism" than in the primary form

Hypercalcaemia may occur whenever calcium salts are being rapidly liberated from bone as in disuse atrophy in rapidly progressing Paget s dis ease especially if the patient is immobilized in bed and when there are widespread metastatic malignant deposits in the bones. Hypercalcaemia is also found in sarcoidosis myelomatosis and in vitamin D in toxication In the first the effect is similar to that of overdosage of vitamin D there is increased absorption of calcium from the gut This is antagonized by cortisone Calcification may occur in various sites particularly in organs secreting acid—that is the pulmonary alveoli the mucous membrane of the stomach and the kidney Even before nephrocalcinosis occurs renal function is reduced and a rising blood urea with tubular failure and polyuria occur

Widespread metastatic calcification may occur in the collagen diseases particularly in dermatomyositis which is probably the commonest cause of calcinosis universalis It may also occur round the joints in rheumatoid arthritis It may also result from the high intake of milk and alkalis in the treatment of peptic ulcer and lead to renal failure and nephrocalcinosis

Hypoparathyroidism

Hypoparathyroidism develops when the glands are removed during thyroidectomy Rarely it occurs in an idiopathic form in which case calcification in the basal ganglia commonly occurs. A very rare form known as pseudohypoparathyroidism seems to be due to a congenital defect of the renal tubules which fail to respond to the parathyroid hormone

Clinical Picture. The sudden disappearance of parathyroid hormone from the circulation after removal of the glands leads to a rise of blood phos phorus The calcium falls in turn and at levels much below 8·0 mg/100 ml tetany occurs There may be paraesthesiae and cramps in the limbs and then spasms of certain groups of muscles occur par ticularly of the forearm producing the main d accoucheur (Trousseau s sign) compression of the arm by inflation of a sphygmomanometer cuff may produce this deformity Chvostek s sign—contrac tion of facial muscles on tapping over the stylomastoid foramen—may be seen Spasm of the larynx and generalized convulsions may occur Tetany may also occur in alkalosis particularly the acute respiratory alkalosis that follows hyperven tilation (p 154) It may occur in rickets and in uraemia though in this case the acidosis of renal failure makes it a rarer event than might be expected. Considerable adaptation often occurs to chronic hypocalcaemia though cataracts may de velop in time

Treatment. Acute cases require the intravenous injection of calcium gluconate Parathormone can be given but usually post operative cases can be controlled by large oral doses of vitamin D Hyper calcaemia must not be produced by overdosage for control the regular testing of the urine with the Sulkowitch reagent (p 148) is a good substitute for frequent blood calcium estimations which need be carried out only if there is a very thick white turbidity Dihydrotachysterol (AT 10) is theoreti cally more efficient than calciferol since its action more closely resembles that of parathormone but in practice good results are obtained with calciferol which is much cheaper

syndromes loss of calcium in the urine leads to hypocalcaemia and osteomalacia One is renal tubular acidosis in which urinary titratable acidity and ammonia are reduced resulting in loss of cations including calcium and potassium in the urine The hypercalciuria may lead to nephrolithiasis and possibly to nephrocalcinosis though it seems probable that the pyelonephritis which is often the cause of this syndrome may be one factor in the aetiology of this renal calcification In the Fanconi syndrome there is a failure of tubular absorption of glucose amino acids organic acids and phosphate so that both calcium and phosphate are lost in increased amounts in the urine

Idiopathic hypercalciuria has been invoked to explain those cases where there is an unexplained loss of calcium in the urine It is important to establish that the ionized calcium in the blood is normal Some cases are due to mild renal tubular damage There are however cases in which no cause can be found and in which tubular calcium reabsorption may be subnormal A high proportion suffer from nephrolithiasis

Symptoms These may be referable to the skeleton with bone pain tenderness and deformities or fractures or to hypocalcaemia which may be severe enough to cause tetany (p 151) or if prolonged cataract formation

Treatment Apart from that appropriate to the cause therapy consists in giving vitamin D The dose required varies from 5 000 units of calciferol a day in rickets to several hundred thousand daily in resistant cases As there is a very real risk of inducing hypercalcaemia renal failure and nephrocalcinosis (p 151) the dose should be cautiously increased with frequent estimations of the plasma calcium Where there is no anomaly of calcium excretion testing the urine with the Sulkowitch reagent serves as a guide a very heavy precipitation is a warning that the blood level is high Renal acidosis should be treated with alkalis (sodium citrate up to 3 g q i d) potassium may also be required

Hyperparathyroidism

Hyperplasia of the parathyroid glands may occur primarily or be secondary to the hypercalcaemia of renal failure and other conditions associated with osteomalacia Adenomas of the glands also occur Though the action of parathormone is complex and is probably exerted both on the bones and the renal tubules the original views of Albright (that the hormone produces a phosphate diuresis by inhibiting tubular reabsorption) offer a satisfactory explanation of the clinical course of patients with hyperparathyroidism The plasma calcium level rises *pari passu* with the fall in phosphate leading to increased urinary calcium loss This may cause nephrolithiasis which in many cases leads to infection and renal failure If the calcium intake is insufficient to maintain balance calcium and phosphate are mobilized from bone and osteitis fibrosa cystica occurs This disease was described by von Recklinghausen in 1891 (though at least two of his cases were of polyostotic fibrous dysplasia p 152) The first successful removal of a parathyroid adenoma was performed by Mandl in 1925

Primary Hyperparathyroidism

The commonest cause is an adenoma of one of the glands In a few cases there is more than one Carcinoma is rare Simple hyperplasia may occur The symptoms are divisible into (1) those due to hypercalcaemia (2) those due to nephrolithiasis and (3) those due to osteitis fibrosa cystica

1 *Hypercalcaemia* The plasma calcium level may be raised to 12 mg/100 ml or higher This is associated with muscular weakness hypotonicity and shortening of the QT interval in the *ECG* Anorexia and constipation are common Calcium may be deposited in the deeper layers of the conjunctiva a lesion more easily seen and diagnostic of hypercalcaemia is the band keratitis in the superficial layers of the periphery of the cornea High levels of plasma calcium produce anomalies of renal function There is polyuria at first (apparently from a direct action of the ion on tubular cells) followed by falling glomerular filtration and rising blood urea Calcification may occur in the renal tubular cells and interstitial tissue causing nephrocalcinosis and in the stomach and pulmonary alveoli

2 *Nephrolithiasis* The high urinary calcium excretion frequently causes the formation of calcium phosphate and calcium oxalate stones in the urinary tract Such patients should always be investigated from the point of view of parathyroid function the Sulkowitch reagent provides a useful screening test Nephrolithiasis and pyelonephritis lead to further renal destruction and this by reducing the phosphaturia may lead to a secondary rise of plasma phosphate and fall of plasma calcium

3 *Osteitis fibrosa cystica* develops in a proportion of cases in which calcium balance has not been maintained by adequate intake Pain in the bones deformities cysts and fractures occur

Diagnosis This should be considered in all cases of unexplained polyuria and renal failure and in

CHAPTER 10

Disturbances of the Body Fluids and Electrolytes

A A G LEWIS

NORMAL FLUID AND ELECTROLYTE BALANCE

The total body water forms 55 to 70 per cent of the body weight in males 45 to 60 per cent in females It is divided between three spaces the intravascular and extravascular compartments of the extracellular fluid (ECF) and the intracellular fluid (ICF) These are not watertight divisions in fact there is a constant interchange of water between them and with the water in the gut as well which is not included in any of them The concept of ECF as a space which has definable limits and of which the volume can be accurately measured is an idealization but is clinically useful provided it is not taken too literally

Water excretion by the kidney can be adjusted within extremely wide limits (from approximately 500 ml to more than 20 times this volume in 24 hr) Losses from the lungs and skin (insensible loss) vary according to atmospheric temperature and humidity but average normal figures are 700–1 000 ml in 24 hr This is rather more than the quantity of water in the solid food of the diet together with that deriving from its combustion so that urine volume depends on the amount of water drunk The obligatory minimum urine volume however is determined by the rate of excretion of urinary solutes

The total body sodium averages 75 mEq/kg of body weight one third being extracellular some of the remainder is available for rapid exchange (1 g NaCl = 17 mEq of Na and Cl) The average diet contains 5–10 g of salt a day Losses of sodium occur in the faeces sweat (which may be regarded as a hypotonic solution of sodium chloride) and urine the latter normally accounting for more than 90 per cent of the intake Sodium can be conserved in the body by the action of adrenal corticosteroids which increase the renal tubular reabsorption of this ion from the glomerular filtrate and so prevent its loss in the urine The kidney can also conserve sodium while excreting large quantities of anion (such as chloride or bicarbonate) the tubular cells reabsorbing sodium and exchanging for it hydrogen potassium or after a time lag ammonium (which they synthesize)

The total body potassium is 40–50 mEq/kg of body weight 98 per cent being intracellular The dietary intake is very variable but averages 100 mEq/day Less than 10 mEq are lost daily in the faeces the rest being excreted in the urine The kidney cannot conserve potassium as efficiently as it can sodium the latter can be almost completely removed from the urine while the concentration of potassium is seldom less in urine than in plasma

Abnormal Losses of Water Sodium and Potassium

These occur mainly from the alimentary tract or in profuse sweating renal disease or pituitary or adrenal deficiency A litre of vomit may contain any amount of sodium and potassium up to 120 mEq of the former and 35 of the latter according to the acidity of the gastric juice By severe diarrhoea a patient may lose 70 mEq of potassium a day and five times as much sodium The drainage of bile or ileostomy fluid causes considerable loss of these cations In chronic renal disease there may be a failure of conservation of water and sodium less commonly of potassium In Addison s disease there is a constant renal loss of sodium with a tendency to potassium retention In diabetes insipidus (p 122) when circulating ADH i deficient there is an abnormal loss of water

In acute renal failure neither water sodium nor potassium can be excreted normally the intake of the former can be reduced to prevent oedema but the catabolism of protein may liberate sufficient potassium to cause cardiac arrhythmias and arrest

Regulation of Acid base Balance

The pH of the body fluids is maintained within narrow limits by a number of buffer systems supported by the action of the lungs and kidneys which vary the alveolar partial pressure of carbon dioxide

Polyostotic Fibrous Dysplasia

This was described by Albright and his associates in 1937 and is therefore often called Albright s syndrome though probably at least two cases were included in von Recklinghausen s description of osteitis fibrosa cystica

There are multiple fibrous areas of rarefied bone with irregular brown pigmentation of the skin and often in females sexual precocity (p 127) The lesions are usually unilateral or segmental Involvement of the bones of the skull may produce a bizarre appearance The blood chemistry is normal No treatment is known

sciousness prevent a normal response to water depletion The great majority of cases of hypertonicity after cerebral lesions fall into the second category

2 *Hypotonicity* may occur if large volumes of water are drunk or given intravenously as glucose solution when they cannot be excreted as in acute renal failure or after a major surgical operation or severe burn Severe water intoxication is rare but mild degrees are probably common in these circumstances

A low ECF sodium concentration usually occurs when there is salt depletion and is found therefore in Addison s disease and in salt losing nephritis But coincident water loss may mask this so that a normal concentration does not rule out the possibility of salt deficiency Conversely hyponatraemia may occur in chronically ill patients without any deficiency when it cannot be corrected by saline therapy

3 *Low ECF volume* occurs in salt deficiency from any cause as in severe sweating diarrhoea and vomiting Addison s disease salt losing nephritis and after severe burns and haemorrhage The blood volume is low cardiac output falls there is tachycardia with a fall of systolic blood pressure and a tendency to postural syncope and the limbs are cold with collapsed veins Thirst may occur even when there is hypotonicity but may be absent The urine is low in volume and concentrated sodium rapidly disappears from it (and chloride as well which may be tested for more simply)

4 *Expansion of ECF volume* occurs when more salt is given than can be excreted This commonly occurs only when renal sodium excretion is greatly reduced as in cardiac or hepatic failure in acute nephritis or tubular necrosis and after large doses of sodium retaining hormones such as desoxycorticosterone The blood volume and venous return are increased and jugular venous pressure rises Oedema is evident clinically when an expansion of more than about 5 litres has occurred If this expansion takes place very suddenly acute pulmonary oedema may occur

Potassium Deficiency

A low ECF potassium usually accompanies body potassium depletion though acidosis dehydration or salt deficiency may mask the low ECF level Hypokalaemia nearly always develops insidiously in patients who are losing large quantities of potassium (by diarrhoea or vomiting from a fistula or in the urine during steroid hormone therapy in Conn s syndrome (p 127) or after major surgical procedures or burns) and who are not taking a normal diet or potassium supplement Potassium deficiency tends to cause apathy anorexia muscular weakness sluggish reflexes and oedema Bowel movements may be reduced and ileus may occur There are usually characteristic changes in the electrocardiogram sagging ST segments low T waves and prominent U waves The diagnosis should not be excluded if these are absent or if the plasma potassium is normal it should be considered whenever the above symptoms occur in a patient known to be losing abnormal quantities of potassium Potassium deficiency is often accompanied by some sodium retention with a tendency to a high ECF bicarbonate and low ECF chloride (hypochloraemic alkalosis ') There is often in chronic cases a failure of renal concentrating power a definite tubular lesion with vacuolation of the cells ultimately develops (hypokalaemic nephropathy)

Hyperkalaemia

The ECF potassium level rises in acute renal failure as the potassium derived from protein metabolism accumulates Hyperkalaemia occurs only in *advanced* chronic renal failure As the ECF level rises apathy and muscular weakness occur with numbness and paraesthesiae in the limbs followed by areflexia and paralysis The latter may affect the respiratory muscles The ECG shows symmetrical peaking of the T waves which become taller as the ECF potassium rises Increasing degrees of heart block and ultimately ventricular fibrillation or standstill occur

Diagnosis and Treatment of Disorders of Body Fluids and Electrolytes

For correct diagnosis three separate guides are available namely the history of the patient s illness and observations on his intake and output in the preceding days examination of the patient and estimations of plasma and urine electrolytes

Every effort must be made to obtain an exact history An estimate must be formed of the patient s intake and losses during the preceding period so that a rough balance over that time can be constructed Even when no exact figures are available a definite opinion can often be formed of the true state of affairs Thus a patient who has had severe diarrhoea for some days and has only taken fluids may very well be deficient of some hundreds of mEq of sodium and potassium A stuporous diabetic with fever and ketosis may need large quantities of water and be suffering from both sodium and potassium deficiency and acidosis as well

In conscious patients thirst is the most important indication of water loss But it may be absent if

and the reaction of the urine While intracellular buffers contribute to the maintenance of the normal pH the most important regulating system is that of bicarbonate/carbonic acid in ECF The Henderson Hasselbalch equation

$$pH = 6\,1 + \log \frac{B\,HCO_3}{H_2CO_3}$$

expresses this relationship The numerator of the right hand term is the concentration of bicarbonate bound base in ECF determined by the renal tubular reabsorption of hydrogen ions in exchange for part of the sodium ions of the glomerular filtrate The denominator is directly proportional to the pCO_2 of arterial blood which is the same as that of the alveolar air Normally $B\,HCO_3/H\,CO_3$ is 20/1 and pH = 6 1 + 1 3 = 7 4

Disturbances of Acid base Balance

1 *Metabolic acidosis* occurs in diabetic acidosis and after administration of large acid loads A highly acid urine is passed with some of the organic acids of ketosis undissociated an increased amount of sodium is reabsorbed to maintain bicarbonate bound base in exchange for hydrogen ions which are buffered in the urine partly by the conversion of HPO_4 to H_2PO_4 Later tubular ammonium formation increases and covers the abnormal anions so that further reabsorption of cation can take place These mechanisms may however be insufficient to prevent acidosis and figures as extreme as 7 0 for pH and 5 mEq/l for ECF bicarbonate may be found In chronic renal disease there is a failure of hydrogen ion excretion and of tubular ammonium formation leading to metabolic acidosis

2 *Respiratory acidosis* may occur in respiratory infections and emphysema pCO_2 rises and compensation occurs with a rise of bicarbonate bound base *if this is insufficient the pH is less than 7 4*

3 *Metabolic alkalosis* occurs after the ingestion of large quantities of alkali or the loss of hydrogen ions by vomiting ECF bicarbonate is high but respiration is depressed to raise pCO_2

4 *Respiratory alkalosis* occurs in hyperventilation which rapidly lowers pCO_2 Tubular exchange of Na for H is at once suppressed and large quantities of bicarbonate sodium and potassium are excreted in a highly alkaline urine In spite of this pH may move rapidly to the alkaline side and tetany may occur from decreased ionization of calcium

It is evident that the ECF bicarbonate may be high or low in either acidosis or alkalosis Both blood pH and bicarbonate should therefore be determined whenever possible for while it may be obvious from the circumstances whether for instance a low bicarbonate is associated with metabolic acidosis or respiratory alkalosis other secondary effects may have occurred to mask this In any case only a direct determination of pH will show to what extent compensation has been successful.

The Regulation of ECF Tonicity

The normal ionic concentration of ECF is 290 mOsmols/litre This level is kept nearly constant by the activity of the supraoptico hypophysial system a rise of tonicity stimulates the secretion of antidiuretic hormone (ADH) which stimulates renal tubular water reabsorption from the glomerular filtrate so that the urine becomes more concentrated The maximum concentration of the urine at a specific gravity of about 1 035 is some four times that of ECF and the minimum 24 hr volume between 400 and 500 ml with a normal diet Rise of ECF tonicity also causes movement of water from ICF and the sensation of thirst If a large volume of water is drunk ECF dilution at once suppresses ADH secretion as the hormone is removed from the blood the urine volume rises to a maximum (10–20 ml/minute) and the ingested water is excreted In this way a litre of water can be drunk and excreted within 4 hr with perhaps 2–5 per cent dilution of ECF for a brief period When ECF tonicity falls water passes into cells if water cannot be excreted and cellular overhydration is considerable water intoxication will occur with headache vomiting convulsions and ultimately death in coma

The Regulation of ECF Volume

Since sodium is the principal ion maintaining ECF tonicity the total quantity of sodium in the body largely regulates ECF volume by the ADH mechanism A sudden *increase in sodium* intake expands ECF volume water being retained at the same time and the excess sodium is removed only slowly It is thought that the secretion of aldosterone by the adrenal is suppressed possibly as a result of the increased blood volume causing a greater venous return to the heart Tubular reabsorption of sodium therefore diminishes and the urinary excretion rises The reverse mechanism seems to operate in sodium deficiency Renal conservation may not be maximal for some days after intake has been greatly curtailed

Disturbances of ECF Tonicity and Volume

1 *Hypertonicity* usually occurs only when water *is not available for drinking* or disturbances of con

concerned in the average adult each litre may theoretically contribute 10 mEq/litre to the ECF bicarbonate bound base In practice ECF sodium is nearly always depleted for other reasons including a loss in the urine which may be continuing so that saline should be given over and above this

In planning oral replacement therapy it is useful to remember that a pint of milk contains 10 mEq of sodium and 18 of potassium and provides about 300 calories In every patient once a plan for therapy has been made a detailed balance chart must be maintained from then on and the totals made up in 12 hourly periods

It should always be remembered that a patient not a laboratory figure is being treated An attempt to correct an isolated abnormality may be futile and do more harm than good In many chronic illnesses for example the plasma sodium tends to be low and the potassium rather high no amount of juggling with the intake will correct these figures

The Action of Diuretics

Osmotic diuretics such as urea act by increasing the amount of unreabsorbed filtrate passing through the renal tubules extra water and sodium being carried away with the osmotic load *Xanthine derivatives* such as Aminophylline increase cardiac output and renal blood flow and to some extent increase glomerular filtration rate and the renal excretion of sodium *Mercurials* mainly inhibit the tubular re absorption of chloride (and in some cases of sodium) The extra chloride is excreted in the urine with sodium and water so that ECF volume is reduced If sodium conserving mechanisms are already maximal the main loss of cation may be of potassium and the sudden potassium loss produced in these circumstances by an injection of mercurial diuretic in a fully digitalized patient may precipitate digitalis toxicity The efficiency of a mercurial diuretic is increased by giving a chloride load just before it if this is in the form of ammonium chloride the ammonium ion is broken down to urea in the liver and the extra chloride excreted with sodium This also tends to prevent the development of hypochloraemia after the prolonged use of mercurial diuretics a condition that may ultimately inhibit the response to them Hyponatraemia may also develop in patients treated too vigorously with mercurials with low ECF volume and a tendency to weakness and vascular collapse (low salt syndrome ') *Acetazolamide* (Diamox) inhibits the action of carbonic anhydrase in the renal tubule The quantity of hydrogen ion available for exchange with sodium is therefore greatly reduced so that much more of the sodium in the glomerular filtrate is allowed to pass into the urine

Chlorothiazide (Saluric) and *hydrochlorothiazide* combine some of the chloruretic properties of mercurials with inhibition of carbonic anhydrase All drugs possessing the latter property will cause the reaction of the urine to become more alkaline and will tend to increase potassium excretion since this ion will largely replace hydrogen in the tubular ion exchange Their continued use may therefore lead to potassium deficiency so that it should be accompanied by a potassium supplement

there is coincident sodium loss and is often severe after a *haemorrhage when it is chiefly the volume of the blood and ECF* that are deficient A dry tongue is an unreliable sign as it is so often produced by mouth breathing An inelastic skin remaining *wrinkled after* being pinched up indicates a loss of ECF associated with this there may be circulatory *signs (p 155)*

The hyperventilation of acidosis may be deep and hissing (Kussmaul breathing) and in diabetes *the sweet* odour of acetone may be obvious

The apathy muscular weakness and depressed *reflexes* of potassium deficiency may be found

Examination of the urine should include an estimate of the 24 hr volume of specific gravity and of *sodium chloride and potassium concentrations* if facilities are available The volume is low and the specific gravity high in dehydration and for a variable period (usually 24 hr) after major surgical operations and severe burns Urinary sodium and chloride concentrations are low for several days after operations and burns at the onset of acute infections and when the patient is forming oedema There may be a difference between the rates of sodium and chloride excretion as for instance after prolonged vomiting when the patient retains chloride rather than sodium Otherwise very low urinary sodium and chloride concentrations in urine of normal or low volume indicate salt depletion Urinary potassium concentration may be raised after operations burns and fractures and may be no lower than the plasma level even in deficiency of this ion

If circulatory collapse has been severe and pro*longed acute tubular necrosis may have occurred* (p 475) which is distinguished from other causes of oliguria by the greater reduction of urine volume with little rise of specific gravity

The blood urea sodium potassium and bicarbonate should be determined as well as the haemoglobin plasma proteins and if possible the pH The blood urea rises in all cases of dehydration (pre renal azotaemia) because of the fall of renal blood flow and filtration rate The plasma sodium and potassium may be low *in deficiencies of those* ions and the sodium may be raised in pure water deficiency but many exceptions to this occur An ECG should be taken

When all the relevant information has become available the physician *should be able to form an* estimate of the nature and extent of the deficiencies present and to plan corrective therapy bearing in mind that continuing losses (including the daily insensible loss of water) must be replaced But very often emergency action has to be taken without these laboratory data and common sense must be relied on Wherever possible and if time allows replacement should be by the oral route for over loading cannot then occur unless cardiac or renal failure have developed

Treatment *Low ECF Volume* After haemorrhage burns or other causes of protein loss the immediate need may be to restore circulating blood volume with blood plasma or dextran Otherwise replacement must be with 5 per cent dextrose or physiological saline according to the requirements judged by the *recent history* The patient who has had diarrhoea and vomiting for some days with signs of dehydration and low systolic blood pressure will need at least 2 litres of intravenous saline Severe hypertension and circulatory collapse indicate a deficit more than twice this The degree of concentration of the haemoglobin and plasma proteins may also give an indication of the deficit if it can be assumed they were normal before dehydration occurred If the plasma sodium level is low the deficiency of sodium in each litre of ECF should be multiplied by the total body water to arrive at the number of mEq of sodium to be given since all body fluids will be hypotonic Once renal blood flow and glomerular filtration have been restored the kidney will correct the abnormalities of body composition and the blood urea will fall Urinary sodium and chloride may be low for some days however In assessing the completeness of body fluid restoration clinical evidence as well as the levels of haemoglobin proteins urea and electrolytes should therefore be considered

Potassium Deficiency No attempt should be made to correct this without laboratory control and *unless it is certain* that there is no renal failure Wherever possible replacement should be oral (1 g KCl = 13 mEq) Intravenous potassium should never be given faster than at 20 mEq/hr and the solution should not be more concentrated than 40 mEq/litre As intracellular losses may be very considerable this form of replacement is somewhat inefficient

Hyperkalaemia occurring in acute renal failure may endanger life The ECF potassium may be *reduced by the injection of large* doses of insulin (causing its deposition with glycogen within cells) by the administration by mouth or as an enema of a potassium free ion exchange resin (Resonium A) by intermittent lavage of the peritoneal cavity *with an isotonic solution containing* no potassium or by the use of the artificial kidney

Acidosis A satisfactory replacement solution is sodium lactate the anion being removed in the body and sodium retained to reconstitute the bicarbonate A *one sixth molar* solution is used which is roughly isotonic as far as the sodium is

ideal weight after the age of 45 If the patient can not curb his appetite 5 or 10 mg of *d* amphetamine sulphate (Dexedrine) an hour before the chief meals will reduce it but even these doses may produce mental excitement and the drug may be habit forming If thyroid is required the patient is suffer ing from myxoedema not from obesity if it is not even large doses will produce little effect

DEFICIENCY DISEASES

To maintain health activity body weight, and growth certain minimum quantities of protein carbohydrates water mineral salts vitamins and calories must be consumed absorbed and normally metabolized Each of these may be separately con sidered but a deficiency of any one of them alone is rare in the great majority of deficiency states several constituents of the diet are below the neces sary minimum In malnutrition due to poverty for example there is usually a shortage of calories pro tein iron and several vitamins

Deficiencies may occur in the following way—

1 *Deficient intake* due to poverty careless choice and preparation of food food fads im pairment of appetite in disease drug addiction and alcoholism anorexia nervosa or when re quirements are increased during growth in pregnancy and lactation in prolonged fever or hyperthyroidism

2 *Impaired absorption* in steatorrhoea and chronic diarrhoea after gastric operations or re section of small intestine in prolonged antibiotic therapy (which also reduces intestinal synthesis of certain vitamins)

3 *Abnormal metabolism or losses* as in Cush ing s syndrome diabetes mellitus prolonged bleeding or albuminuria and extensive burns

The effects of deficiencies of water iron iodine calcium phosphorus sodium potassium and vita min B_{12} are dealt with elsewhere in this book

Undernutrition

The Food and Agriculture Organization of the United Nations recommends 3 200 calories daily for 25 year old 65 kg men who are moderately active in a temperate climate with 2 300 calories for women of 55 kg These standards are high and are above those attained by very large numbers of the inhabitants of underdeveloped countries In the diets of these people it is nearly always in protein that the deficiency is greatest This is true also in the poorest sections of wealthier countries not only because the cheapest diets contain the least protein but because less will be available for growth and tissue repair when the calories necessary for energy are not largely supplied by fat and carbohydrate One gramme of protein per kg body weight daily is enough for normal adults if the diet is mixed it will contain enough first-class protein and essential amino acids even if entirely lacto vegetarian A greater intake is desirable in the first year of life in pregnancy and lactation and in convalescence from any prolonged illness

When the diet is deficient in protein apathy weakness and fatigue develop insidiously Fatty in filtration and fibrosis of the liver anaemia hypo proteinaemia and oedema osteoporosis and spon taneous fractures may occur There is reduced resistance to infections particularly tuberculosis It may take a long period of high protein feeding with extra milk meat and cheese to restore the depleted tissue proteins to normal Casilan is a use ful source of extra protein which has the advantage when there is oedema of being salt free In some chronic wasting diseases in which it is difficult to maintain a positive nitrogen balance for any length of time the implantation of 200 mg of testosterone subcutaneously or administration of Nilevar orally (which has the protein anabolic effect of testosterone without its androgenic effect) may stimulate protein anabolism and assist in this

When protein deficiency is associated with a shortage of calories body weight is lost but is eventually stabilized since the basal metabolism and body temperature are reduced and muscular weak ness an aversion to any physical effort and easy fatiguability all combine to reduce energy expendi ture The skin becomes rough and may be pig mented and covered in fine hair the extremities are *cold and oedema may occur before there is detect* able hypoproteinaemia There is a tendency to hypotension and postural syncope Fatty infiltration of the liver does not occur since the fat depots are depleted at an early stage Varying degrees of vita min deficiency are often associated and there may be scurvy or a haemorrhagic tendency In more rapid starvation however there is often an in creased tendency to venous thrombosis

The treatment of chronic severe malnutrition must not be too vigorous The ability to absorb fat is impaired and large meals are badly tolerated Skimmed milk extra protein in the form of Casilan glucose and a vitamin supplement may be given in frequent feeds of as much as the patient can tolerate

CHAPTER 11

Nutrition and its Disorders

A A G LEWIS

OBESITY

A ROUGH guide to a patient's ideal weight when dressed is obtained by taking 114 lb as the average for a woman of 4 ft 11 in and 128 lb for a man of 5 ft 2 in and adding 3 lb for every extra inch for a woman and 4 lb for a man Even allowing for differences in build the weight should not differ from the average by more than 10 per cent and this figure should not increase with age Any patient whose weight is greater than this is obese and has during some period ingested more calories than were necessary for the maintenance of this ideal weight Normally food intake is very exactly adjusted to calorie requirements by a hypothalamic centre and body weight may remain constant for many years Variations in energy expenditure necessitate corresponding changes in calorie intake for this to be achieved but in the majority of normal adults these variations are not great and it has been shown that thin people may in fact expend less energy than many fat people in performing the same tasks Considerable variations also occur in the basal metabolic rates of different people but obese patients usually do not have low BMRs and anything more than mild obesity is seldom a feature of myxoedema Once the patient has become obese slothfulness and the protection afforded against heat loss by the extra fat may reduce the number of calories required to maintain constant weight The calorie intake may not then seem so very excessive

Obesity is therefore the result of the ingestion of more calories than were required at some time in the past There is no evidence that if the causes of oedema are excluded the extra weight is ever due to water though obese patients may fail to lose weight for a time when given low calorie diets because of temporary sodium and water retention In all cases the excess weight is due to the deposition of fat in fat cells and it is the distribution of these that cause the variations in contour of obese people Apart from the characteristic distribution of body fat in the female and the tendency of patients with Cushing's syndrome to deposit fat on the face and trunk there are no specific endocrine patterns of obesity

The increase of appetite leading to obesity results very rarely from a hypothalamic lesion when it may be associated with retarded sexual development (Frohlich's syndrome p 140) The great majority of fat boys suspected of having this syndrome are in fact merely greedy and are found to have genitalia of normal size though the penis may be partly obscured by suprapubic fat The adrenal hormones stimulate appetite and so cause obesity in Cushing's syndrome it seems probable that they may be responsible for the hearty appetite that maintains moderate obesity in some physically vigorous adults Usually however gross obesity is one expression of a faulty psychological and physical adjustment to life After a severe emotional disturbance several pounds may be gained every week Many women gain weight rapidly at the menopause when they may feel that their most active years are past and may lack other forms of sensual satisfaction The vehemence with which very obese patients often deny that their food intake is excessive and their insistence that weight is being maintained on a starvation diet indicate a bizarre lack of insight

Treatment Sufficient calorie restriction will invariably reduce weight The majority of co-operative patients merely need to be given the following instructions—

1 Eat no fat and no fried foods

2 Take no more than one slice of bread or one potato at each meal

3 Eat no sweets preserves sugar cakes or pastry

Lean meat half a pint of milk salads green vegetables and fruit are allowed each day Increased co operation can be obtained by pointing out that hunger nearly always diminishes after a few days of perseverance and by the reminder that mortality increases by 10 per cent for every 10 lb above the

sense are reduced or absent and there is peripheral sensory loss In wet beri beri tachycardia raised venous pressure oedema and effusions into serous cavities occur A cerebral form also occurs (Wernicke s encephalopathy) with nausea and vomiting ocular palsies agitated depression in somnia and amnesia

Treatment in the early stages with oral or paren teral vitamin B_1 in doses of 10–50 mg produces a rapid improvement in all recent cases of beri beri Chronic cases however improve much more slowly and yeast or Marmite should be given to provide the whole of the B-complex

Vitamin B_2 (Riboflavin)

Vitamin B_2 acts as a coenzyme in hydrogen transfer for oxidations It is present in milk meat and flour Two mg daily is an adequate supply

Riboflavin deficiency causes cheilosis a glossitis of a magenta hue seborrhoeic dermatitis and some malaise weakness and loss of weight

Nicotinic Acid (Niacin)

Nicotinamide (Niacinamide) occurs in the tissues in the nucleotides coenzymes I and II which act as carriers for hydrogen released by dehydrogenases The acid and its amide are found in liver kidney yeast and to a lesser extent in meat wholemeal flour green vegetables and peanuts Ten to twenty mg are required daily

Pellagra results from deficiency of this vitamin It is endemic in the Southern states of U S A and in some countries of Southern and Eastern Europe The mucous membrane of the tongue mouth oeso phagus and stomach becomes red swollen and ulcerated A burning sensation is followed by nausea vomiting and diarrhoea A red itching desquamating type of dermatitis d velops on areas of the skin exposed to light and friction Depres sion and intellectual impairment occur and there may be mania Peripheral neuritis may develop The conditions responds to oral or parenteral nicotin amide (up to 500 mg daily) though Marmite or yeast and a high protein diet should be given as well

Vitamin C (Ascorbic Acid)

Vitamin C is water soluble and largely destroyed by cooking (unless done anaerobically) and by alkalies Black currants strawberries citrous fruits Brussels sprouts cauliflowers cabbages tomatoes and new potatoes are the best sources There is little in milk and pasteurization reduces the amount Seventy five mg daily is an adequate intake—twice this amount is desirable in pregnancy and lactation

Ascorbic acid is needed for the formation of inter cellular ground substance in deficiency there are defects of the protein matrix of bone and the linings of capillaries and wound healing is delayed

Scurvy occurs after a prolonged period of vitamin C deficiency Normal adults deprived of the vitamin for 5 months developed the disease ascorbic acid could not be detected in the plasma for 14 weeks before this or in the white cells for 3–6 weeks before A plasma level of 0 1 mg/100 ml excludes the diag nosis while a white cell content below 2 mg/100 ml supports it These estimations form a more reliable guide to the diagnosis than saturation tests based on urinary excretion

As the disease develops enlargement and kera tosis of hair follicles is seen with coiling of the hair inside them later these follicles become haemor rhagic Swelling and haemorrhages occur in the gums Extensive subcutaneous and muscular hae morrhages may occur while bleeding from mucous membranes and cerebral haemorrhages are less common Anaemia osteoporosis and delayed wound healing occur in the chronic condition

In infantile scurvy which is rare in breast fed infants unless the mother is deficient in vitamin C there is a failure to thrive and gain weight Sub periosteal haemorrhages follow very mild trauma often at the lower end of the femur Lesions of the gums subcutaneous and orbital haemorrhages and bleeding from mucous membranes occur Fever anaemia and dyspnoea are common

The condition responds to large doses of vitamin C up to 1 g being given orally or parenterally daily

Vitamin D

A number of steroids possess the property of increasing the absorption of calcium and phos phorus from the bowel and so preventing rickets Vitamin D_2 (calciferol) and vitamin D_3 (present in fish liver oils and formed in the skin under ultra violet irradiation) both have this effect The inter national unit for vitamins in this group is 0 025 μg of crystaline vitamin D one teaspoonful of cod liver oil contains 350 units the amount required by an average infant daily

Rickets the result of an insufficient supply of vitamin D is characterized by a wide irregular zone of ossification at the growing ends of bones with excessive provisional calcification (p 149) The serum calcium is except in severe cases normal the serum phosphorus is reduced and the alkaline phosphatase raised The disease now rare in Western Europe and the U S A occurs in infants between the ages of 4 months and 2 years being

at a time a more solid mixed diet can be given later When food cannot be given by mouth an attempt must be made to give the necessary calories intravenously but the results are disappointing A mixture of 10 per cent glucose protein hydrolysate and a fat emulsion can be given but the first is liable to cause venous thrombosis a good deal of the nitrogen of the second is excreted in the urine and the third even if available is liable to cause severe reactions in a proportion of cases A certain amount of alcohol can be included to provide extra calories but it is difficult to maintain normal nutrition for any length of time by the intravenous route let alone restore it in a deficiency state

Kwashiorkor

In tropical countries protein deficiency is common in the presence of an adequate calorie intake it is often made worse by malaria hookworm infestation and schistosomiasis or by toxic substances in the diet such as ragwort (senecio in South Africa) The name Kwashiorkor which originated in the Gold Coast is now used to describe a syndrome found with local variations in large parts of Africa India and South and Central America Children are usually affected between 6 and 18 months after weaning the diet being almost entirely carbohydrate during a time of rapid growth Diarrhoea oedema a red desquamating dermatitis starting on the buttocks and groins and soft *pale hair are characteristic* Muscle wasting fatty liver anaemia and hypoproteinaemia occur The condition is cured by a diet of skimmed milk cirrhosis and hepatic venous occlusion may develop if it progresses

Anorexia Nervosa

Anorexia nervosa is a condition in which an abnormally low weight results from the intake of insufficient calories Ninety per cent of cases occur in young women There is frequently a history of preceding emotional stress A number of patients give a history of being overweight before the onset and become abnormally thin as a result of change of dietary habit adopted to overcome this In spite of being underweight the patient is often extremely active She may in the ward devise many expedients to hide or dispose of food Amenorrhoea occurs early in the disease but the breasts and the body hair are preserved and the latter may be increased in distinction to hypopituitarism Hypotension osteoporosis and spontaneous fractures may occur, pulmonary tuberculosis may develop

The treatment is by psychotherapy but the prognosis is bad Successes have been claimed for prefrontal leucotomy Endocrine therapy is useless

Vitamin Deficiencies

Vitamin A

Vitamin A is fat soluble and heat stable occurring in fish liver oils and dairy products It is also formed in the liver from the carotene group of pigments which are present in vegetables fruit and cereals in amounts roughly proportional to the intensity of their green or red colour

Adults probably need 3 000 I U daily twice this amount may be required during growth pregnancy or lactation Requirements are increased in steatorrhoea obstructive jaundice and liver disease

Vitamin A deficiency causes a loss of visual acuity in dim light and follicular keratosis Night blindness xerophthalmia and keratomalacia occur in *severe deficiency*

Vitamin B_1 (Thiamine Aneurine)

Vitamin B_1 is water soluble and heat stable occurring *in* the germ and bran of cereals in pulses and in much smaller amounts in meat milk and vegetables The phosphorylated vitamin *acts* as a coenzyme *in the* decarboxylation of carboxyacids during the *metabolism* of carbohydrate The requirements increase with *greater energy* expenditure and when more carbohydrate is being utilized Some thiamine is synthesized by intestinal bacteria *Two mg is probably a sufficient daily* intake under all conditions but the vitamins of the B group are closely associated and it is unlikely that deficiencies *occur singly*

Thiamine deficiency leads to accumulation of pyruvic acid in the nervous system and the blood *with chromatolysis* of nerve cells and degeneration *of medullary sheaths* Peripheral nerves and the vagi *are affected also The heart* is dilated there is tachycardia with a hyperkinetic circulation and later a *high output type of* failure The linical syndrome *is known as beri beri* dry and wet types *being distinguished* according to the predominance *of neurological* or cardiac abnormalities *though* mixed types are common

Beri beri Intellectual impairment emotional instability loss of appetite fatigue *and paraesthesiae* occur before the full syndrome *develops In dry* beri beri there is a peripheral neuritis *affecting the legs more than the arms with loss of sphincter* control late in the disease Burning paraesthesiae *severe* cramps and muscular weakness occur the calves are tender tendon reflexes and posterior *column*

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A number of steroids possess the property of increasing the absorption of calcium and phosphorus from the bowel and so preventing rickets Vitamin D_2 (calciferol) and vitamin D_3 (present in fish liver oils and formed in the skin under ultra violet irradiation) both have this effect The international unit for vitamins in this group is 0 025 μg of crystaline vitamin D one teaspoonful of cod liver oil contains 350 units the amount required by an average infant daily

Rickets the result of an insufficient supply of vitamin D is characterized by a wide irregular zone of ossification at the growing ends of bones with excessive provisional calcification (p 149) The serum calcium is except in severe cases normal the serum phosphorus is reduced and the alkaline phosphatase raised The disease now rare in Western Europe and the U.S A occurs in infants between the ages of 4 months and 2 years being

entirely preventable by a dietary supplement of vitamin D or by regular exposure to sunlight The affected infant is irritable and has flabby hypotonic muscles deformities of the skull (with flattening of the occiput and areas of bony softening) of the thorax (pigeon breast rickety rosary due to prominence of the costo chondral junctions) and of the legs and pelvis occur Treatment consists in the addition of fish liver oil to the diet physiotherapy and orthopaedic measures may be required to correct deformities Tetany and laryngismus due to low serum calcium are rare complications of severe rickets

Hypervitaminosis D may occur whenever very large doses of vitamin D are given to correct a deficiency of this substance or in the therapy of certain conditions (such as tetany or lupus vulgaris) There is an excessive absorption of calcium and phosphorus from the bowel leading to high blood levels and eventually to metastatic calcification particularly in the renal tubules (nephrocalcinosis) Death from uraemia may occur The urine of any patient receiving large doses of vitamin D should be regularly tested with the Sulkowitch reagent a very thick white turbidity indicates a high calcium excretion and therefore a raised blood level

Vitamin K

Vitamin K (K_1 and K_2) is fat soluble It occurs in plants and eggs and is synthesized by intestinal bacteria It is necessary for the hepatic formation of prothrombin a deficiency of the vitamin leads to a lowered prothrombin concentration a prolonged prothrombin time and a haemorrhagic diathesis Deficiency arises only through impaired absorption from the intestine in obstructive jaundice biliary fistula steatorrhoea and small intestinal insufficiency Probably there is impairment of both formation and absorption of the vitamin in the new born being sometimes severe enough to cause the haemorrhagic diathesis 5 mg of Menaphthone (Menadione Sodium Bisulfite U S P) should be injected intravenously or intramuscularly if bleeding is due to malabsorption of Vitamin K A similar dose given to pregnant women the day before delivery prevents haemorrhage in the new born

Vitamin E

Vitamin E has been claimed to be effective therapeutically in a large number of conditions There is no conclusive evidence of its value or of its role as a vitamin in human nutrition

CHAPTER 12

Storage Diseases Sarcoidosis

A A G LEWIS

Amyloidosis

In amyloidosis an abnormal protein-carbohydrate complex is deposited in various tissues This substance is not as once thought chondroitin sulphuric acid it is probably not of fixed composition and its characteristic metachromatic staining with aniline dyes is variable in degree

In the very rare *primary* form of the disease which occurs in middle age the abnormal substance is deposited mainly in the walls of small arteries particularly in the skin mucous membranes muscles lungs liver spleen and kidneys Macroglossia and localized amyloid tumours may occur The cause is unknown Ten to twenty per cent of cases of multiple myeloma develop primary amyloidosis but there is no relationship with any other condition

Secondary amyloidosis may complicate a large number of chronic diseases in which suppuration or tissue destruction occur particularly tuberculosis bronchiectasis osteomyelitis and ulcerative colitis It may also rarely occur in rheumatoid arthritis The extensive use of anti bacterial therapy has greatly reduced its incidence the condition is reversible The liver spleen kidneys and adrenals are most often involved

The diagnosis rests on the discovery of amyloid deposits in a biopsy specimen usually taken from skin muscle liver kidney or the gum In secondary amyloidosis there is always an obvious predisposing condition and the staining reaction with methyl violet is more constant and characteristic than in the primary form Antemortem diagnosis of the latter may be impossible if only one organ is involved cardiac amyloidosis for example may present with unexplained cardiac enlargement and failure The use of Congo Red in diagnosis based on the fact that amyloid takes up this dye and causes its rapid disappearance from the circulation is unreliable owing to the difficulty of standardizing the normal result

Glycogen Disease

Excessive deposition of glycogen in liver kidney and heart with a failure of glycogenolysis is a rare congenital abnormality It may be hereditary The cause is unknown but is presumably the absence of an enzyme

In the hepatic form the liver is enlarged The diagnosis is made by biopsy Spontaneous hypoglycaemia and ketosis occur and frequent carbohydrate feeds are therefore necessary

In the cardiac form cardiac enlargement and failure occur As macroglossia is common primary amyloidosis may be suspected Treatment is confined to that of cardiac failure

Lipidoses

Lipids may be deposited in the cells of certain organs in three conditions namely Gaucher s disease and Niemann Pick s disease (the lipids being kerasin and sphingomyelin respectively) and xanthomatosis (cholesterol) The latter is usually associated with a raised level of blood cholesterol occurring in hereditary hypercholesterolaemia idiopathic hyperlipaemia diabetes mellitus chronic obstructive jaundice and the nephrotic syndrome it may however occur with a normal blood cholesterol level as one stage in the progression of histiocytic reticulo endotheliosis

Gaucher s disease is a rare condition with a hereditary tendency Kerasin is deposited in cells of the reticulo endothelial system giving them a characteristic appearance In children and adults the spleen and bone marrow are mainly involved the former often becoming huge Splaying of the lower end of the femur is common and pathological fractures may occur hypersplenism may cause anaemia leucopenia and thrombocytopenic purpura Brownish pigmentation of the skin and brown wedge shaped thickenings of the conjunctivae (pingueculae) may be found In infants the disease takes a widespread rapidly progressive form involving particularly the nervous system In adults there may be few symptoms apart from abdominal discomfort or purpura when splenectomy is indicated

Niemann Pick s disease is a rare progressive fatal disease of infants It is usually hereditary and is much commoner in Jewish families There is

widespread deposition of sphingomyelin throughout the reticulo endothelial system with enlargement of lymph glands spleen and liver destruction of the nervous system and of the bones and anaemia and leucopenia No treatment is effective

Hereditary hypercholesterolaemia is a rare condition transmitted as a Mendelian dominant The levels of free cholesterol cholesterol esters and phospholipids in the blood are raised but not that of neutral fat Those members of a family affected show an increasing tendency to develop atheroma and xanthomatous lesions as they grow older Myocardial infection and intermittent claudication are common Xanthelasmas yellowish plaques may be found on the eyelids (they occur also in normal people) Orange yellow tuberous xanthomas may be found on the buttocks and on the extensor surfaces of the elbows and knees Xanthomas may also be felt as nodules on tendons

Idiopathic hyperlipaemia which is only occasionally hereditary is a rare condition The blood levels of cholesterol phospholipids and neutral fat are all raised Eruptive cutaneous xanthomatosis occurs the yellowish papules appearing anywhere on the body (including the lips and palate) but most often on the buttocks and extensor surfaces of the limbs Tendon xanthomas may occur but not xanthelasmas There is hepatosplenomegaly and attacks of severe abdominal pain occur which may be associated with pancreatitis

In *hypercholesterolaemia* due to other causes cutaneous xanthomatosis takes the eruptive form This is now rarely seen in diabetics The liver is enlarged

Histiocytic reticulo endotheliosis is probably a neoplastic process running a very variable course and occurring in infants children and young adults Varying degrees of xanthomatous infiltration cellular reaction and eventual fibrosis occur and three main types of the disease are usually recognized though there are many transitional forms between them

1 *Letterer Siwe disease* is an acute disseminated form occurring in infants and usually fatal There is a maculo papular rash enlargement of liver spleen and lymph glands and a miliary type of pulmonary infiltration It is possible that cortisone may sometimes control this condition

2 *Eosinophilic granuloma of bone* occurs in young children An area of bone destruction is visible in the X ray often with periosteal new bone formation The diagnosis is established by biopsy Spontaneous healing is the rule

3 *Hand Schuller Christian syndrome* (normo cholesterolaemic xanthomatosis) is the commonest form of the disease in children and young adults The lesions particularly affect the long bones and the skull appearing in the X ray of the latter as clear cut areas of bone destruction Cellular tumours may cause exophthalmos pituitary destruction with diabetes insipidus or facial deformities Miliary pulmonary dissemination may occur and healing by fibrosis may lead to the development of honey comb lungs Cutaneous xanthomas may occur as yellow or brown nodules anywhere on the body but particularly on the neck and in the axilla and antecubital fossa (xanthoma disseminatum) The lymph glands liver and spleen may also be involved and enlarged

Tumour masses in bone should be curetted or irradiated the latter may prevent progressive pituitary destruction Involvement of the lungs may cause spontaneous pneumothorax and eventually death from pulmonary heart failure

Haemochromatosis

Haemochromatosis (Bronzed Diabetes) is a rare chronic disease in which abnormal iron absorption leads to an increase in the body stores of iron and the deposition of iron containing pigments (mainly haemosiderin) in many tissues The liver spleen skin lymph glands adrenals pancreas and skin are the organs mainly affected The disease is very rare in women in whom there is a regular iron loss by menstruation (Chronic haemolysis and repeated blood transfusions may cause the deposition of haemosiderin in some organs but this rarely leads to functional disturbances)

Clinical Picture The skin becomes the colour of slate occasionally adrenal deficiency causes the deposition of melanin as well The liver and spleen enlarge and multilobular cirrhosis and symptoms of hepatic failure develop Fibrosis of the pancreas causes diabetes mellitus

Diagnosis The combination of pigmentation cirrhosis and diabetes mellitus is diagnostic A skin biopsy confirms the presence of haemosiderin The serum iron concentration is above the normal upper limit of 180 μg/100 ml

Treatment Hepatic or adrenal failure and diabetes are the complications usually requiring treatment An attempt should also be made to lower the body iron stores by the removal of a pint of blood a week this seems to be successful in halting the progress of the disease

SARCOIDOSIS

Sarcoidosis is a chronic disease of unknown cause producing often in a number of organs a characteristic histological picture Granulomas are found composed of epithelioid tubercles containing multinucleated giant cells without evidence of caseation or necrosis Certain other conditions such as tuberculosis syphilis berylliosis brucellosis histoplasmosis leishmaniasis leprosy and metastatic malignant disease may produce the same histological changes in organs commonly affected by sarcoidosis

The disease is commonest in youth and middle age in temperate climates It affects rural populations more than urban (unlike tuberculosis) and in North America it is commonest in Negroes It often produces characteristic clinical syndromes by affecting groups of organs simultaneously

Clinical Picture Often there is little constitutional disturbance but fatigue anorexia sweating arthralgia and low fever may occur Skin lesions occur in nearly half the patients either acutely in the form of erythema nodosum or as a chronic nodular or reddish blue indurated eruption particularly on the face and ears (Boeck s sarcoid lupus pernio) These lesions do not ulcerate but may result in atrophic scars or keloid forming The mucous membranes may be affected Acute or chronic iridocyclitis or uveitis may occur The lacrimal or parotid glands may be painlessly enlarged (uveoparotid fever is one form of the disease) leading to Sjogren s syndrome Enlargement of lymph glands liver and spleen is common Involvement of the central nervous system with meningitis destruction of the neurohypophysis (with diabetes insipidus) or cranial nerve palsies occurs Calcium absorption from the gut may be increased leading to hypercalcaemia metastatic calcification nephrocalcinosis and renal failure

The blood picture may show a moderate anaemia occasionally there is leucopenia or a moderate monocytosis or eosinophilia The α and γ globulin fractions of the plasma proteins are increased and there is a raised E S R The Mantoux reaction even at low dilutions is commonly negative X rays of the chest may show enlargement of the mediastinal glands often with lobulated masses at both hila infiltration of the lung fields may produce a reticular or nodular appearance or later diffuse fibrosis The periphery of the fields tends to be relatively spared and involvement of the pleura and effusions are less common X rays of the hands and feet occasionally show cystic areas in small bones

The general tendency in the majority of patients is for the disease to run a chronic course and to heal slowly often producing fibrosis The latter may lead to progressive reduction of pulmonary function and to pulmonary heart failure or to blindness or glaucoma

Diagnosis This rests ultimately on finding the histological appearance of sarcoidosis in a biopsy specimen from affected tissue and by excluding other causes Skin lymph gland conjunctiva liver and tonsil are the tissues most likely to yield diagnostic material In practice a reasonably confident diagnosis can usually be made from consideration of the clinical picture alone A cutaneous test (the Kveim test) which is said to be specific but which is not yet fully evaluated may confirm the diagnosis An emulsion of sarcoid tissue from a lymph node is injected intradermally when a red nodule again of sarcoid tissue develops in a few weeks in patients with active disease

Treatment The majority of patients need no treatment beyond general measures such as good nutrition and the avoidance of fatigue The only agents that modify the course of the disease are the steroid hormones and these should be given to those with hypercalcaemia progressive pulmonary disease or ophthalmic involvement Local injection or instillation of hydrocortisone is sufficient to control anterior uveitis in all other cases oral treatment is indicated and should be continued in sufficient dosage to control the activity of the disease as judged by clinical pathological and radiological evidence

CHAPTER 13

Diseases of the Alimentary Tract

C F HAWKINS

Introduction

THE variety of the contents of the abdominal cavity the alimentary canal the visceral organs the mesentery and so on provide a wide variety of clinical problems Sometimes the pattern of symptoms is unmistakable as with ulcer dyspepsia or gall stone colic Often the outline is less clear and may be blurred by the personality of the patient for there is no system in the body where the organs react more strongly to emotional stress It is a borderland where functional disorder merges into organic disease a mistaken label of neurosis may be perilous yet an unwarranted organic diagnosis may cause unnecessary invalidism and surgery and deprivation of the enjoyment of eating Whatever the condition the supreme diagnostic tool is the history and dividends are paid when extra care and time are taken over this Sometimes a symptom is specific such as the spontaneous nocturnal pain of duodenal ulcer more often from an accumulation of evidence a circumstantial diagnosis is built up—to be proved or disproved by examination investigations and the effect of therapy

PAIN

Abdominal pain is a common symptom of disorders of the alimentary tract and can also be the most difficult and baffling complaint that a doctor has to treat ranging from the acute and dramatic severity of the abdominal catastrophe to vague syndromes such as chronic pain in the right iliac fossa The site of the maximum pain is important In peptic ulcer this lies in the upper abdomen and pain occurring below the level of the umbilicus is seldom if ever due to this nor should gall bladder disease be diagnosed if much pain occurs in the left side and similarly pain of colonic origin is referred to the lower abdomen The quality of the pain is not helpful except in diagnosing colic where the cycles occur in a crescendo-diminuendo fashion every few minutes and in separating organic from psychogenic pain which is often described as a superficial burning with feelings of pressure and is continuous Organic pain is intermittent and diagnosis depends upon its relation to food or defaecation the effect of alkalis together with associated symptoms such as vomiting jaundice or diarrhoea A thorough and detailed analysis of abdominal pain prompts the diagnosis in most cases and not only saves unnecessary investigations but also avoidable laparotomies

Peptic Ulcer

The pain from a peptic ulcer especially in the duodenum usually pursues a striking and constant pattern It is epigastric as a rule but may occur in the back or elsewhere when somatic structures have been invaded Usually precise in its relationship to food it is relieved by eating or drinking fat intolerance is often noticed by the patient The freedom from pain following an alkali is a useful therapeutic test and the disturbance of sleep by spontaneous pain in the early hours of the morning is a valuable diagnostic symptom Yet the explanation of this has been the subject of controversy for many years since the stomach and duodenum are relatively inaccessible to experimental study Hypotheses have therefore flourished and accumulation of facts has been slow

Observations upon patients undergoing laparotomy under local anaesthesia show that no pain arises from manipulation of normal intestine but that pain can readily be produced by squeezing the inflamed tissues of a gastric ulcer or by stimulating it with chemical agents This proves the existence of pain fibres in the stomach and it seems that local inflammatory changes in and around the ulcer have

lowered the pain threshold to stimuli that are not felt elsewhere in the stomach Hydrochloric acid is the most important stimulant of ulcer pain It has been demonstrated frequently that the introduction of 200 ml of 0 5 per cent hydrochloric acid into the stomach will produce the typical distress in most ulcer patients and no disturbance in a normal patient The pain can be terminated by the with drawal of the acid or the introduction of alkali *through the stomach tube The acid hypothesis is* the only one that can explain the relief of pain by a large meal by a teaspoonful of alkali by aspirating the gastric contents and from vomiting the common factor being the removal of hydrogen ions from the stomach There is much evidence to refute the concept that the usual cause of ulcer pain is muscle tension from abnormal motility But some patients describe their pain as intermittent and cramp like rather than constant and gnawing it is probable that peristaltic movements may excite pain *from the ulcer* and cause *the epigastric pangs of* hunger so familiar to the duodenal ulcer patient Yet many features of ulcer pain remain unexplained such as its absence in some patients in spite of high acidity the rapid relief resulting from bed rest although little if any alteration takes place in the gastric acidity and the insensitivity of the pain producing mechanism that precedes clinical healing

The answer probably lies in the factors that alter the pain threshold Wolf and Wolff (1943) have pro duced evidence that inflammation and tissue damage can alter the visceral pain threshold (as it does in the skin) so that a stimulus that produces no sensa tion in normal tissues may evoke pain when applied to damaged tissues Direct observations upon the stomach of their experimental subject Tom with the gastric fistula indicated that the threshold of *pain—and therefore for the occurrence of gastro* intestinal symptoms—varied with the condition of the mucosa When vascular engorgement inflam mation and oedema were present minor stimuli applied to the mucosa as well as vigorous contrac tions of the stomach are felt The more engorged the mucosa the less forceful was the contraction necessary to cause the pain They stated that a stimulus that did not elicit symptoms under one set of circumstances might do so under another This variability in the pain response may explain dis *crepancies found in experimental work Indeed* much of the mystery of visceral pain disappears when the significance of the lowered pain threshold is realized It is not difficult then to understand that the normally insensitive bowel becomes sensitive to acid in the presence of an ulcer and its accompany ing inflammation and that peristalsis touch or pressure may also evoke painful sensations

Pain in the Right Iliac Fossa

The right iliac fossa is a common site for pain This pain is usually of chronic type and presents much difficulty in exact diagnosis a fact that has resulted in the right iliac fossa being a most notorious area for unnecessary surgery It is a clinical axiom that pain which starts in the right iliac fossa is unlikely to be due to appendicitis though there are exceptions to this as to every other rule

Causes

The Appendix There are three definite clinical syndromes due to inflammation of the vermiform appendix

1 *Acute Appendicitis* The initial pain which is sudden in onset and often severe is due to disten sion of the appendix from inflammatory changes and is referred to the central abdomen or epigas trium Later with peritoneal involvement the pain changes in character and becomes localized to the site of the appendix in the right iliac fossa it either remains there or becomes generalized if peri tonitis develops

2 *Recurrent Subacute Appendicitis* This is due to recurring attacks of mild inflammation In the earlier episodes the pain begins in the epigastrium or umbilical region and settles down in the right iliac fossa but in later ones this shifting character is often absent and the pain is felt in the iliac fossa from the beginning

3 *Recurrent Appendicular Colic* The pain is felt around the umbilicus the reference site of small in *testine pain although guarding and tenderness may* be felt in the right iliac fossa The pain is spasmodic and the bouts of colic may last for a few days these may be due to blockage of the lumen of the appen dix by a faecolith

In all these conditions the pain is intermittent with periods of freedom between attacks It is very doubtful if continuous pain in the right iliac fossa is ever due to the appendix A normal looking appendix may be removed for this and often an obliging pathologist reports some doubtful change that is either a variation of normal or coincidental Usually the same pain continues after removal of the appendix It may in some cases disappear but this may not be regarded as proof that the appendix was at fault for pains of functional origin may

respond to organic measures The diagnosis of chronic appendicitis should not be *made*

Mesenteric Glands Enlargement of glands in the right iliac fossa is a common cause of pain particularly in children There may be tenderness and muscle guarding without rigidity Constitutional symptoms may or may not be present It is difficult to diagnose without laparotomy and often impossible to differentiate between *non specific* mesenteric adenitis and tuberculous adenitis without microscopy of a gland

The Caecum Gaseous distension of the caecum is described as one cause of chronic pain in the right iliac fossa and the physical signs of this are said to be a tympanitic note on percussion gurgling and a doughy feeling on palpation and excessive *peristaltic* sounds on auscultation These signs must depend upon the degree of filling of the caecum by ileal contents and it is difficult to know the variations of normal It is said that such caecal distension may result from constipation in which case the pain should be related to bowel movements or disappear with cure of the constipation It is also thought that such localized pain in the right iliac fossa may be part of colon spasm (*see* p 199) proof of this theory would be obtained by relief of the pain by antispasmodic agents such as atropine compared with results from placebos

The Terminal Ileum Crohn s disease (regional ileitis) may cause attacks of pain in the right iliac fossa resembling appendicitis and from narrowing of the terminal ileum cause episodes of intermittent obstruction Many patients with Crohn s disease *have in fact had their appendices removed during* the course of their illness There may or may not be any constitutional symptoms such as fever or loss of weight at this stage

Female Pelvic Organs Gynaecological conditions are a fairly common cause of pain in either iliac fossa but should be considered only if the pain bears a definite relationship to the menstrual cycle or if there is some associated disorder of menstruation or definite objective abnormality However there may be no association between the pain and *the gynaecological finding and such pain* associated with a vaginal discharge does not for example justify a diagnosis of salpingitis

The Urinary Tract Chronic pyelitis stone in the ureter and hydronephrosis may *all cause pain in* the right iliac fossa Microscopy and culture of the urine will usually detect cases of pyelitis and frequency of micturition will be complained of Pain arising from a ureteric calculus usually radiates from the loin to the groin but may be localized to the iliac fossa when a stone becomes impacted in the *ureter Chronic or* intermittent hydronephrosis may be difficult to diagnose when the pain is not in *the loin as urinary symptoms* may be absent and if it is not palpable diagnosis may depend upon radiological investigations

The Spine Conditions in the spine such as caries deformities or osteoarthritis are rare and frequently obvious causes of pain in the right iliac fossa This usually radiates around from the back and is altered *by movements and posture*

Chronic Pain of Undetermined Origin The cause of most cases with chronic pain in the right iliac fossa remains indefinite in spite of investigation This syndrome is almost confined to adults and is more common in women The description of the pain is a continuous aching or nagging with *occasional sharp stabs It is unaffected by eating* defaecation micturition posture or movement but is worse when the patient is worried or fatigued It is likely that such cases are hysterical rather than organic and it is interesting that the description given of their pain is identical to that seen in cardiac neurosis where there is a continuous ache in the left breast and praecordium Many patients with the aching in the right iliac fossa have an underlying fear of appendicitis or other disease and this fear may have been perpetuated by the doctor s colourful suggestion of a *grumbling appendix* Organic disease seldom produces continuous pain Diagnosis of the nervous origin of this pain is supported by the presence of pains and anxiety symptoms elsewhere but it may exist as a single symptom in women who show no neurotic traits Discussion with the patient may or may not reveal *some emotional cause Provided* a firm line is taken at the onset many patients will be cured following proper reassurance

The Biliary System and Pancreas

Whereas most cases of peptic ulcer are readily diagnosed by the history alone this may not be so with diseases of the gall bladder and pancreas In the classical instance of gall bladder disease *with* stones there are crescendo attacks of agonizing biliary colic in the epigastrium or right hypochondrium with pain reference to the right scapula This pain—a distension pain—is due to a blocked cystic duct and a gall bladder contracting to overcome the obstruction Later a superficial localized pain *develops and is accompanied by* tenderness and muscular rigidity due to irritation of the overlying inflamed peritoneum The diagnosis is clinched if jaundice results Many patients with gall bladder disease do not have this typical *pattern and* radiology of the gall bladder is necessary If this shows disease the case must be reviewed and the evidence reassessed as to whether the gall bladder is the real

cause of symptoms or coincidental For it is a fact that many older female patients have symptomless gall bladder disease and many persist with identical symptoms after removal of the gall bladder Experimental stimulation of the pancreas gives similar pain to that from the biliary tract either in the right hypochondrium or elsewhere depending upon the site in the pancreas—either head body or tail

HEARTBURN AND WATERBRASH

Heartburn a common symptom is an intense and unpleasant substernal burning It is intermittent and immediately relieved by an alkali such as sodium bicarbonate This may occur in normal people when highly irritating liquors are drunk but does not occur when decinormal hydrochloric acid is drunk or gastric content regurgitated unless oesophagitis which lowers the pain threshold is present A striking example of the last is hiatus hernia where a defective cardia allows free regurgitation of gastric juice into the oesophagus this occurs especially when the patient lies or bends down and results in the postural heartburn which is pathognomonic of the condition Heartburn from oesophagitis also occurs following total gastrectomy where the irritant is the small intestine contents rather than hydrochloric acid Many cases of heartburn are associated with peptic ulcer but it is on the whole a non specific symptom that is frequently seen in the absence of structural disease of the upper gastrointestinal tract and then is probably due to oesophageal spasm

Waterbrash less common is a sudden filling of the mouth with saliva This reflex salivation is similarly a non specific symptom It may be associated with peptic ulcer but often occurs in the absence of organic disease

APPETITE

Appetite is a pleasant sensation related to previous experiences of the smell and taste of food whereas hunger is disagreeable and associated with epigastric hunger pains produced by contractions of the empty stomach together with vague general symptoms such as weakness and malaise It is not clear whether appetite and hunger are different degrees of the same sensation nor is the pathogenesis of either understood Appetite bears no correlation with the needs of the body and the amount of food eaten by man which depends on social and environmental factors and is usually greater than his needs Increased appetite is caused by the following—

1 The appearance and smell of food which are important factors in encouraging the convalescent patient to eat

2 Fresh air and exercise

3 Psychological factors

4 Aperitifs like sherry and bitters such as gentian

5 A drug such as insulin

6 Certain diseases like thyrotoxicosis

Pathological increase in appetite (bulimia) is a psychiatric disorder

Diminished appetite occurs as follows—

1 It is an expected symptom of many diseases particularly with fever and may be an early indication of a growth of the stomach

2 Loss of appetite with much fastidiousness about food is often part of the make up of the neurotic patient It is common experience that distressing news causes anorexia and if bad news is given to a patient during a barium meal examination a sudden decrease in gastric tone may be demonstrated

3 A drug such as amphetamine will depress the appetite and the hunger can be relieved without calorie intake if synthetic cellulose compounds which create bulk by being hygroscopic are given instead of food

Loss of appetite sufficient to cause death from starvation occurs in anorexia nervosa a condition that can be difficult to distinguish from pituitary failure (Simmonds s disease) in the later stages Anorexia nervosa is of psychogenic origin and usually occurs in young girls The emotional upset may be obvious and it may respond to simple measures of encouragement Others may need psychiatric help These patients may resort to gross deception to avoid eating and a nurse must usually be present during meals to encourage and sometimes force eating Eating is largely a habit and has to be reformed in these patients

VOMITING

Vomiting is a symptom of so many diseases that it is of little value in differential diagnosis But a detailed analysis and inspection of the vomit may be of great help in certain gastro intestinal disorders The following aspects should be considered—

1 If more than one person develops it and it starts suddenly the possibility of food poisoning or similar infective origin should be explored Sudden

vomiting may be the herald of acute specific fevers in childhood or appendicitis

2 Vomiting is usually preceded by nausea The typical effortless cerebral vomiting unassociated with nausea is more common in posterior fossa lesions particularly when there is involvement of the brain stem and medulla

3 Vomiting which immediately relieves abdominal pain is strongly suggestive of an organic cause such as a peptic ulcer

4 Morning vomiting is commonly due to pregnancy It is frequent in alcoholics where the vomit consists mainly of mucus which has collected in the oesophagus overnight from an alcoholic oesophagitis or in catarrhal subjects where the mucopus induces retching Uraemia is another cause

5 Large amounts of vomit suggest obstruction in the alimentary tract such as pyloric stenosis The *specific symptom of this is the presence of food in* the vomit which has been taken many hours or even a day before

6 Vomiting should be assumed to be of organic *origin There are however certain patients where* it is of nervous origin A characteristic feature is the good nutrition in spite of a long history of months or sometimes years and it occurs durin or immediately after meals

The vomit is precious and must always be kept for inspection Where oesophageal obstruction such as achalasia of the cardia is present the vomit will be alkaline and contain obvious particles of undigested food With pyloric obstruction hydrochloric acid together with remnants of food taken hours beforehand will be *present* but there is usually no bile as it cannot be regurgitated back from the duodenum When the obstruction is below the ampulla of Vater the vomit is biliary and some*times faecal The appearance of blood in the vomit* depends upon the rapidity of bleeding If quick the blood is bright red but if slow or retained in the stomach for some time the haemoglobin is *converted into haematin and the vomit resembles* coffee grounds Vomit containing dark green bile may closely resemble that containing blood but the green colour of bile becomes apparent on diluting with water

DIARRHOEA

Diarrhoea is usually due to some disorder localized to the alimentary tract and only occasionally to diseases elsewhere such as thyrotoxicosis or uraemia It is better defined in terms of consistence of the stools which are semi solid or liquid rather than by their frequency In practice frequency of bowel action accompanies looseness

Acute Diarrhoea Food poisoning by organisms of the staphylococcal or salmonella group is the commonest cause and careful enquiry usually reveals other causes In certain people indiscretion in eating or allergy to particular foods may produce diarrhoea Sudden diarrhoea also results from the use of oral antibiotics due to direct irritation or fungus infections from change in intestinal flora or from operations such as partial gastrectomy Other causes are aperients or poisoning from heavy metals such as arsenic

Chronic Diarrhoea Probably the most frequent cause for the gradual onset of diarrhoea especially if associated with frank or occult *blood* in the stools is a growth of the colon or rectum and this must always be considered first Ulcerative colitis gives a similar onset but the patients themselves have usually noticed obvious *blood in their stools* and proctoscopy gives a diagnostic appearance Diverticulitis pelvic abscess and regional ileitis may present with diarrhoea

Diarrhoea frequently *occurs with no structural* disease of the alimentary tract Steatorrhoea is a strong possibility if there is *associated soreness* of the tongue or macrocytic anaemia Other cases are due to a rapid passage of food through the intestine There may be an increase of the gastrocolic reflex so that frequency of bowel action appears particularly after meals and especially in the morning In these as with nervous diarrhoea where there is a similar rapidity of food transit it is seldom if ever that the patient has to get up *at night* to defaecate

Spurious Diarrhoea This is seen in severe cases of constipation where the rectum is loaded with a mass of faeces that cannot properly be expelled A repeated soiling of the underclothing and the frequent passage of small quantities of stool give a false impression of diarrhoea It is the equivalent of retention of urine with overflow

No patient with diarrhoea is properly examined without a rectal examination which allows of immediate diagnosis of rectal carcinoma or spurious *diarrhoea Inspection of the stool is also* a necessity and may at once result in a diagnosis of steatorrhoea or ulcerative colitis Occult blood tests on the stools distinguish between ulcerative lesions causing *diarrhoea and those due to disturbances* of function such tests if negative may be of more value in excluding a growth of the colon than X ray studies which can be very unreliable

Microscopy and bacteriology of a fresh stool taken before antibiotics have been given is essen

tial particularly in acute diarrhoea Pathogenic organisms and parasites have to be excluded and pus cells searched for Sigmoidoscopy is done whenever neoplasm of the lower bowel or ulcerative colitis or amoebic dysentery is suspected The type of radiological investigations depends upon the particular case If a colonic origin suggested by lower abdominal pain or fresh blood in the stools is considered likely a barium enema should be arranged Otherwise a barium progress meal is the best approach Routine barium sulphate should be used as a flocculation of this indicates a diagnosis of steatorrhoea (*see* p 189) films should be taken at half hourly intervals for 2 hours or longer and when indicated by X ray screening so that the rate of passage of barium through the intestine can be assessed In idiopathic steatorrhoea the barium passes through the small intestine slowly but if the diarrhoea is due to rapid transit from nervous or other causes the barium may reach the colon in 30 minutes and filling of the stomach small intestine and colon by barium may be seen in a single film

SIGNS ON EXAMINATION

Abnormal signs in the abdomen are frequently conclusive of a particular disease and their discovery depends upon the technique of examination as well as upon the experience of the clinician The patient must be relaxed flat and warm and the belly adequately illuminated Careful inspection should never be neglected as a distended stomach may be seen rather than felt and visible peristaltic waves may be diagnostic of obstruction either at the pylorus or elsewhere in the alimentary tract Such waves may however be seen in the normal thin person from movements of the small intestine The examining hand must be gentle and warm beginning at a distance from any expected painful area True tenderness is constant and must be distinguished from the tenderness of the nervous patient which is often widespread and disappears when the attention is directed elsewhere The proof that a lump is in the abdomen rather than in the abdominal wall is obtained by making the patient raise his head when the contraction of the recti muscles results in the disappearance of an intra abdominal lump

If any abnormal structure is detected its size consistency mobility movement on respiration and regularity must all be elicited from it The following normal structures may be palpable in healthy people the liver right kidney descending colon aorta and lumbar vertebrae stools in the colon and particularly in women a distended bladder—or perchance a pregnant uterus No abdominal examination is complete without palpation of the hernial orifices and genitalia in the male Rectal examination should rarely be missed A rectal carcinoma is a tumour that can be felt at an early operable stage and many lives would be saved if the rectum was palpated in every case of diarrhoea or other bowel disturbance

RADIOLOGY

There is no natural contrast medium in the abdomen (as in the chest where the lung structure is outlined by the presence of air) so that a contrast material such as barium has to be introduced before pictures of the alimentary tract can be obtained Plain films therefore help little but may be indicated as follows to detect radio opaque calculi in the gall bladder pancreas or urinary tract to detect air or gas under the diaphragm in suspected perforation of the gut and in obstruction where the air in the gut may provide helpful pictures

Barium studies are accurate in detecting disease in the oesophagus provided suitable techniques are used when indicated Oesophageal varicose veins from portal obstruction are only seen with a thick paste of barium allowed to pass slowly down and hiatus hernia is usually missed unless the patient is tilted in the head down position A considerable proportion of peptic ulcers are not visualized radiographically so that a negative barium meal X ray neither excludes an ulcer in the stomach nor in the duodenum Nor should a negative barium meal be accepted if the clinical diagnosis points strongly towards a carcinoma of the stomach Lesions of the small intestine can similarly be missed which being so long is not surprising special preparations of barium which do not flocculate are needed to outline the mucosal pattern (*see* p 189) The barium enema X ray visualizes the colon and terminal ileum in most cases It may be negative in early cases of ulcerative colitis in spite of extensive mucosal involvement on the other hand an ahaustral narrow descending colon is frequently seen in healthy people and does not necessarily indicate colitis inflation with air after evacuation of the barium often gives beautiful pictures of the mucous membrane and allows more exact diagnosis Most neoplasms of the colon are diagnosed radiologically but those in the caecum and ascending colon are easily missed particularly when faeces obscure the outlines Therefore while a positive X ray is of immense value in the diagnosis of lesions in the alimentary tract a negative report does not prove that disease is absent

The Mouth

The tongue is subject not only to certain local disorders such as neoplasm *tuberculosis* and syphilis but also may give information concerning general disorders—anaemias steatorrhoea dehydra tion and scarlet *fever Inspection* of this organ is traditional and has for long been regarded as a valu able part of the *clinical* examination but more im portance has been attached to this in the past than is justified *Coating of the tongue* due to thickening of the epithelium associated with some debris from bacteria *and food particles* is unconnected with any gastro intestinal disorder or constipation and results *from* mouth breathing from the use of bland diets where chewing is unnecessary and is expected in any *fever* or respiratory tract infection It is com mon in normal healthy people particularly smokers and cannot be regarded by itself as a sign of any *ill health* It gives no symptoms and needs no treatment In contrast the smooth and often painful tongue (glossitis) where the surface is denuded of papillae and perhaps epithelium is frequently an atrophy caused by deficiency of substances essential for the metabolism of healthy cells such as iron vitamin B_{12} folic acid and other vitamins of the B group such as riboflavin nicotinic acid and *pantothenic acid* The smooth tongue occurs there fore in hypochromic microcytic anaemia pernicious anaemia and the steatorrhoea syndrome—a con dition where faulty absorption of food from the small intestine can result in malnutrition with de ficiency of any of these substances Vitamin deficiencies arising in normal people from defective food intake are rare in this country and usually seen only in elderly bachelors or spinsters living alone or in lunatics who refuse to eat normal food

The tongue should be moist and dryness is a useful sign of dehydration of the body provided local factors causing drying such as mouth breath ing and diminution of the normal buccal secretions from the parotid and submaxillary glands are ex cluded Sjogren s syndrome is a rare disorder where there is a failure of secretion from the mucous glands of the buccal mucosa and from the salivary glands and is sometimes associated with dryness of other mucous surfaces such as in the respiratory tract and conjunctivae The cause is unknown and there is at present no treatment Geographical tongue is a condition seen in many normal tongues and is characterized by slightly *raised irregular grey* rings surrounded by reddish areas The condition comes and goes and may make the tongue painful but is more often symptomless It is of no clinical significance and no treatment is of effect except anaesthetic lozenges for relieving pain The benign nature of geographical tongue contrasts with leukoplakia which is a whitish thickening of the mucosa of the tongue or cheek and is probably a pre malignant condition Black tongue (lingua nigra) is a state where the papillae over the posterior portion of the tongue are greatly elongated and may appear black or brown The aetiology is un known It is symptomless and difficult to eradicate *and all that is needed is reassurance of the pati nt*

The tongue so easily inspected by its owner is an organ from which neurotic symptoms commonly arise Cancerophobia is induced by worry concern ing the shape and the size of the papillae Pricking and burning sensations may occur and many intro spective people study their tongues in the mirror each morning using this as a barometer to foretell their feelings for the day the greater the coating the worse they are Cure is effected by simple ex planations of the normal oral physiology and by persuading them not to look at their tongues

TEETH AND GUMS

The importance of teeth is that they should be efficient from the mechanical aspect so that the food can be ground sufficiently and so prepared for swallowing and digestion Sepsis associated with teeth plays little if any part in general medical disorders and the days have fortunately gone where total extraction of the teeth frequently followed the diagnosis of rheumatoid arthritis peptic ulcer and vague syndromes such as fibrositis or being run down The exception to this is bacterial endo carditis and careful attention to the teeth is abso lutely necessary for all patients with rheumatic valvular disease extractions should be done under a cover of penicillin to eliminate the *Streptococcus viridans* that may be released into the circulation during the extraction Otherwise a conservative approach to retain teeth for as long as possible is indicated Dentures should be provided when mechanical inefficiency develops or local disease makes extraction necessary these must be well fitting or the patient takes them out to eat o swallows air because of the oral discomfort and so develops flatulent dyspepsia

The commonest disease of the gums is pyor rhoea an inflammatory condition of the gingival tissue and peridental membrane Secondary infec

tion of the alveolar bone occurs This condition is easily diagnosed clinically whereas apical abscess is usually detected radiologically Certain general dis orders give specific changes in the gums scurvy a dietary deficiency of vitamin C occasionally seen in elderly people who live alone results in swelling and bleeding of the gums and responds to ascorbic acid therapy epileptics receiving phenytoin show a somewhat similar hypertrophy of the gums which may be so marked as almost to bury the teeth but it differs from scurvy in its microscopical picture and failure to respond to ascorbic acid and is of no significance A blue line near the margin of the gums is diagnostic of lead or bismuth poisoning

Stomatitis

Inflammation of the mouth can result from the ingestion of many external irritants These may vary from highly spiced foods and excessive alcohol or tobacco consumption to the corrosive poisons taken by suicides A common cause of stomatitis today is the use of oral antibiotics such as penicillin tetra cycline and others the exact explanation is un known but it may be due to some disturbance of the bacterial flora of the mouth and it is usually best to discontinue the antibiotic or to give it parenterally Simple catarrhal stomatitis also occurs during the course of fevers or in debilitated patients where it may be prevented by careful oral hygiene It is seen during the eruption of the first teeth in children or in association with gross sepsis of the teeth in adults and may be a sign of poison ing by heavy metals such as bismuth lead arsenic mercury or gold Such cases of stomatitis may cause only discomfort rather than pain to the patient and are diagnosed by the reddening of the mucous membrane Symptomatic treatment consists of mouth washes or regular cleansing by the nursing staff by sodium bicarbonate or hydrogen peroxide and swabbing with glycerine and lemon

Specific types of stomatitis are—

Thrush (Parasitic Stomatitis) This is due to the yeast like fungus *Candida albicans* which forms whitish patches on the mucous membrane of the mouth tongue or pharynx these may coalesce to form an easily detachable membrane which when wiped off leaves a bleeding excoriated surface Diagnosis is confirmed by the typical appearance of mycelial threads under the microscope Thrush is seen in infants where the infection may be trans mitted from dirty feeding bottles but also occurs in adults particularly during debilitating illnesses such as cancer or ulcerative colitis It seldom leads to serious trouble It responds to a saturated solu tion of sodium bicarbonate either by hourly mouth wash or direct application Alternatively the thrush can be moved by gentle swabbing and the area painted with a 1 per cent aqueous solution of gen tian violet three times daily for about three days

Ulceromembranous Stomatitis (Vincent s Angina or Trench Mouth) This is an infectious and con tagious condition involving the oral and pharyngeal mucosa and in particular the gums Painful super ficial ulcers covered with a whitish grey membrane occur with much inflammatory induration of the surrounding tissues Removal of the necrotic tissue leaves a bleeding surface The breath is foul and fever may be present with enlargement of lymph nodes dysphagia occurs when the pharynx is in volved Vincent s organisms and fusiform bacilli are present in large numbers and are probably the cause of the condition though it must be remem bered that these can occur in normal mouths The disease responds to penicillin

An identical appearance of ulcerative stomatitis may be seen in blood dyscrasias such as leukaemia agranulocytosis or aplastic anaemia and these should be excluded by examination of the blood Certain drugs—phenylbutazone and the heavy metals—also cause this disorder without neces sarily any change in the white blood cells

Ulceromembranous stomatitis must be dis tinguished from the anginal type of glandular fever which presents with a white adherent membrane in the tonsillar fossae or on the soft palate There is usually much constitutional disturbance with enlargement of glands and spleen The blood films are usually characteristic with increase of mono cytes and atypical lymphocytes and the Paul Bun nell test becomes positive after a week or two of the illness Diphtheria gives a similar membrane with enlargement of cervical lymph glands There is little or no inflammatory reaction around the membrane and the breath has a sweet scented odour which can be recognized by those accustomed to seeing this disease The severity of the consti tutional symptoms contrast with the slight pyrexial reaction The appearance of *Corynebacterium diphtheriae* in throat swabs is diagnostic

Ulcers

Traumatic ulcerations in the mouth may be due to badly fitting dentures from biting the cheek or other injuries They heal quickly when the cause is removed If single ulcers persist in the mouth for longer than three or four weeks the possibility of carcinoma should be considered Both the malig nant and syphilitic ulcer are painless whereas the tuberculous type is more often painful and follows open tuberculosis in the lungs

Recurrent simple ulcers in the mouth (aphthous stomatitis) is a condition seen in all age groups

and particularly in women of middle age The ulcers which may start as vesicles are small—2 or 3 mm in diameter—superficial and very painful particularly on eating or drinking Crops of these ulcers come and go for no apparent reason they heal spontaneously and intervals of freedom from trouble lasting many months may follow although the condition may persist for years No cause has been found for the condition which is usually a *local* disease confined to the mouth and unconnected with other gastrointestinal disorders Nor has any treatment been found effective The patient has to be reassured and protected from unnecessary measures such as dental extractions Anaesthetic lozenges containing amethocaine or similar drug can be used before eating It is probable that the majority of cases subside spontaneously Herpetic stomatitis a form of herpes simplex similar to the fever blisters on the lips may give similar painful ulcers after the vesicles have ruptured but are confined to one side of the mouth and do not cross the mid line Pemphigus may be confined to the mouth before the skin manifestations develop and presents as blisters which rupture and leave shallow painful ulcers usually larger than in aphthous stomatitis This is frequently fatal but may respond to corticosteroids Other diseases involving the skin which may give ulceration in the mouth are lichen planus where whitish areas resembling leukoplakia may break down with subsequent superficial ulceration and the Stevens Johnson syndrome where symmetrical papular or vesicular skin lesions occur with involvement of the conjunctiva and buccal mucous membrane In the mouth it starts with bullous or vesicular lesions which change into superficial ulcerations leaving a curious crusting of the lips It is a self limiting disease of unknown origin and is a severe variant of erythema multiforme

Fordyce s disease is a term used when the mucous membrane of the mouth has a speckled appearance because of the mucosal glands and is a normal variation of no significance

SALIVARY GLANDS

The main function of the saliva which is produced at the rate of about a litre daily is a mechanical one It aids mastication and swallowing facilitates speech and helps to dilute irritants and to cool excessively hot foods It also has a weak and unimportant digestive action in the hydrolysis of starch due to the enzyme ptyalin which may continue in the stomach until stopped by contact with the hydrochloric acid which neutralizes it The flow of saliva depends upon intact parotid and submaxillary glands and the usual stimulus to secretion is the sight smell or thought of food

Hyposecretion or Dry Mouth (Xerostomia)

The dry mouth due to nervousness is a physiological event. Otherwise this symptom is uncommon in apparently healthy people The presence of diminished secretion should always be confirmed objectively by examination of the mucosa of the mouth and in particular the flow of saliva from the opening of the parotid duct inside the cheek (opposite the second upper molar tooth) after stimulation by the smell of lemon or massage of the parotid glands themselves Xerostomia is an expected event in febrile conditions or in states of dehydration such as diabetes mellitus Addison s disease or whenever diarrhoea is present It is a common side effect of the atropine group of drugs and the synthetic anti-cholinergic agents Dry mouth from diseases of the salivary glands is unusual, and diagnosis is not difficult as these glands are so easily examined by palpation Sjogrens syndrome is a rare condition which when severe gives rise to gross and incapacitating dryness so that swallowing and speech become impossible without lubrication from water or acidulated sweets which have to be sucked constantly It is an atrophy of unknown origin affecting the mucous secreting glands of the mouth and sometimes respiratory tract together with diminished lacrimation It usually fails to respond to pilocarpine or cholinergic drugs

Hypersecretion (Ptyalism)

Increased salivation may be caused by irritative lesions in the mouth such as sepsis of the gums or buccal mucous membrane A reflex salivation due to disturbances in the stomach or duodenum such as peptic ulcers may result in *waterbrash* a striking symptom where the mouth is suddenly and unexpectedly filled with the typical clear salivary fluid Ptyalism may precede vomiting It also occurs in pregnancy and may be a functional symptom in the visceral neuroses Excessive salivation sometimes occurs in affections of the mid brain and pons which cut off the hypothalamus from the salivary nuclei as in encephalitis lethargica it may indeed be a troublesome feature of post encephalitic Parkinsonism This however must be distinguished from sialorrhoea due to an inability to swallow the normal flow of saliva or the drooling of saliva in imbeciles The treatment of ptyalism consists in removal of the cause wherever possible Atropine or similar drugs can be used and X ray therapy to the salivary glands should be considered

only when the symptom is incapacitating and unresponsive to other measures

Parotitis

Mumps is the specific disease affecting the parotid glands and should always be suspected when there is a sudden painful and unexplained enlargement of one or both of these glands It is the commonest disease and should be considered in all age groups Diagnosis may be supported by the presence of leucopenia and an increase in the number of lymphocytes Involvement of other glands—the testes ovaries and pancreas—may occur together with meningitis

Acute infections with pyogenic organisms such as the streptococcus are uncommon but are always a possible complication in moribund patients The organisms may reach the salivary glands through the ducts or in other cases from the blood stream There may be much pain with trismus there is high fever rapid pulse and a leucocytosis Pressure on the affected gland may induce a purulent discharge through the duct Treatment is by antibiotics and measures to drain pus if necessary

Chronic or intermittent enlargement of the salivary glands may present a difficult clinical problem Some cases may be from pyogenic infections or may be due to calculi—a condition more likely in the submandibular glands Calculi in the ducts may be felt and X rays probing of the ducts and sialographs (with lipiodol) may help in the diagnosis Tumours such as the mixed parotid tumours are easily separated from the chronic enlargements of benign origin involving the whole gland There is however a group where exact diagnosis may be impossible and even a biopsy may not give a precise answer Mikulicz s disease is a rare condition affecting the salivary and lachrymal glands the enlargements consist of firm painless swellings without systemic symptoms Aetiology is unknown and treatment unsatisfactory but it is said that X ray therapy may be effective Some cases are part of a general disorder such as leukaemia lymphosarcoma or sarcoidosis

The Oesophagus

Disorders of the oesophagus present less difficult clinical problems than in the rest of the alimentary tract This is due to its relative simplicity as it is a hollow muscular tube about 25 cm long which conveys the bolus of food to the stomach following its preparation in the mouth It does this by active peristalsis rather than by gravity proof of which is obtained by the ability of a person to swallow while standing on his head Abnormalities of this neuromuscular mechanism are concerned in achalasia of the cardia and perhaps in certain cases of otherwise unexplained dysphagia Sensations from the oesophagus readily reach consciousness The warm feeling behind the sternum after swallowing hot liquids is a common example more intense stimuli are described as heartburn a symptom that occurs in oesophagitis but also in the absence of any structural disease in the oesophagus or stomach Other stimuli result in severe substernal pain identical with that of coronary artery disease this has been proved by balloon distension of the lower oesophagus in patients with angina—they are unable to distinguish this pain from their customary angina Obstructive lesions of the oesophagus which is the only pathway for ingested food give severe nutritional disturbances with rapid emaciation and death from starvation if the condition is unrelieved

Accurate diagnosis can often be obtained from the history alone Examination of the oesophagus by routine clinical methods is impossible but any vomit or regurgitated fluids should be studied and the absence of gastric juice or digestion of the food confirmed Radiological diagnosis is usually exact but it may be necessary for the patient to be examined lying down to eliminate the speedy passage of the barium or to use thicker mixtures of a barium paste to outline lesions of the mucous membrane The fundus of the stomach must also be examined to exclude a carcinoma invading the cardia a condition which is easily missed In doubtful cases oesophagoscopy will provide a complete inspection of the entire oesophagus and biopsies can be taken or strictures dilated

Dysphagia

Difficulty in swallowing is a precise and specific symptom and should never be ignored It is ominous in later life and often indicates cancer starting with solids the difficulty increases so that fluids may be brought back in later stages (*see* page 200) In all age groups achalasia of the cardia and hiatus hernia represent benign causes of dysphagia

Difficulty in swallowing may present as an emotional symptom in neurotic people In others it results from oesophageal spasm without structural disease but this diagnosis should never be made without a complete barium swallow examination also a blood count to exclude the Plummer Vinson syndrome seen in iron deficiency anaemia

Inflammatory diseases of the mouth or pharynx

such as stomatitis tonsillitis quinsy or tuberculous laryngitis may give dysphagia but the primary dis ease is usually obvious This also applies to tumours or the numerous conditions in the neck or thorax which by pressure may obstruct the oesophagus—goitres enlarged glands growths of the lung or mediastinum aneurysms etc

Dysphagia may also be a prominent and dan gerous symptom of various neurological disorders such as bulbar paralysis myasthenia gravis diph theritic neuritis and others It is due to involve ment of the pharyngeal muscles and a fatal inhalational pneumonia may occur unless feeding through a stomach tube is instigated at once

Oesophagitis

Acute oesophagitis is the natural sequel to the ingestion of injurious substances such as boiling water foreign bodies and corrosive or heavy metals like iron (when children mistakenly swallow ferrous sulphate tablets for sweets) It may also be an extension from acute pharyngitis and occur in various fevers The pathology shows varying de grees of inflammatory changes with necrosis of the mucous membrane in severe cases and stricture formation if the patient survives There may be much retrosternal pain particularly on swallowing Once the traumatic agent is removed healing will take place this may be hastened by temporarily feeding by other routes such as a stomach tube or intravenously

Chronic oesophagitis is the more common clinical problem It may result from the continued drinking of some irritating substance like alcohol the morn ing vomiting of the alcoholic is usually a regurgi tation of a mucous catarrhal fluid which has collected in the oesophagus during the night Other types of oesophagitis are those produced in the lower part of the gullet from the regurgitation of fluids upwards through the cardia The oesophagus i lined by squamous epithelium and is not equipped to withstand the corrosive effects of the gastric and intestinal secretions Normally the cardia is the guardian against regurgitation of gastric contents

It is unusual for reflux to occur in normal people where the anatomy of the cardia is intact and hiatus hernia is the commonest cause of this type of oesophagitis Yet there is little doubt that repeated vomiting from pyloric stenosis or pregnancy may result in similar changes and repeated bathing of the lower oesophagus by gastric juice may take place in conditions where there is increased intra abdominal pressure as in obesity ascites and pregnancy These may be the start of persistent inflammation in the absence of a definite hernia

Although heartburn is most often a functional dis turbance of the oesophagus the possibility of oeso phagitis should always therefore be considered, and oesophagoscopy carried out to exclude it if neces sary The pathological changes are those of red dening and oedema of the mucosa with superficial ulceration particularly along the crests of the verti cal rugae the ulcers may be covered by a grey sloughing membrane which on its removal leaves a bleeding surface In the chronic phase stenosis follows the ulceration Sometimes fibrous strictures without any inflammation are seen suggesting that spontaneous healing can take place Malignant change is thought not to occur

The mechanism of the cardia as a valve is com plex There is a weak sphincter formed by the muscle of the lower oesophagus but regurgitation is mainly prevented by the acute angle at which the oesophagus enters the stomach Any rise in the intra gastric pressure tends to increase the efficiency of this mechanism (as happens with the entry of the parotid ducts into the mouth) The crura of the diaphragm are important in maintaining the sharp angulation of the lower end of the oesophagus and the fibres of the right crus which twist around the margins of the oesophageal hiatus exert a pinch cock action which is lost when a hernia is present There are two main groups of hiatus hernia (*see* Fig 13 1) the sliding type which is reducible into

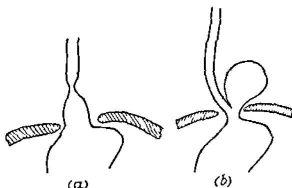


Fig 13 1 Hiatus Hernia
(*a*) Sliding type (*b*) Paraoesophageal type

the abdomen if not tethered by surrounding ad hesions and the paraoesophageal or rolling type The essential difference is the angle at which the oesophagus enters the stomach in the sliding type the cardia is patulous and ineffective so that symp toms are frequent in the paraoesophageal one the cardia is frequently still efficient and symptoms are less likely

Diaphragmatic Hernia

Herniation of the stomach through the oesophageal hiatus of the diaphragm is the commonest and most important type of diaphragmatic hernia other varieties are traumatic hernias from severe injuries and anterior protrusions through the foramen of Morgagni which are rare Hiatus hernia may be seen in infants when it gives rise to an effortless vomiting sometimes blood tinged or gastro intestinal haemorrhage Most cases however appear in later life with symptoms of oesophagitis and it is impossible to know how long the actual hernia has been present but the occasional presence of congenital abnormalities perhaps suggest a similar origin in some instances It is probable that pregnancy with its increase of intra abdominal pressure accounts for some cases and that a similar rise in this pressure explains the association of obesity with hiatus hernia

Symptoms. Many patients with hiatus hernia go through life without symptoms so that it may exist as a coincidental finding Sometimes the complaints are quite specific such as postural heartburn on bending or lying down at night Substernal pain and difficulty when swallowing food or drink may occur More often the symptoms are those of any non specific dyspepsia and the radiologist s discovery of a hernia comes as a surprise careful judgment is needed to be as certain as possible that the symptoms are due to the hernia a condition that is not infrequently associated with duodenal ulcer or gall bladder disease An iron deficiency anaemia may be the first and only symptom and results from chronic blood loss due to the bleeding from the associated ulceration of the lower oesophagus These peptic ulcers may cause haematemesis and occasionally perforate Continued ulceration leads to fibrosis and shortening of the oesophagus—the more likely explanation of cases previously described as congenital short oesophagus The final outcome may be a stricture and this can present without previous dyspeptic symptoms

Diagnosis Objective confirmation of the clinical diagnosis is obtained from the radiologist The condition may be missed in the routine barium meal as adequate tilting of the patient in the head-down position with pressure on the abdomen is essential and bending forward movement may be necessary to demonstrate oesophageal regurgitation An ulcer crater may be demonstrated Endoscopy can be used when indicated to confirm the associated oesophagitis or peptic ulcer

Treatment Hiatus hernia in infants is treated by nursing them in an upright position thickening the feeds and giving them a semi solid diet as soon as possible Most children lose all their symptoms when they start walking Surgery offers adults the most effective treatment and is indicated if the symptoms are persistent and the patient is fit enough repair of the hernia also prevents the complication of oesophagitis such as stricture formation The results of surgery are good but, as in other herniae there is a small recurrence rate

Medical treatment is directed towards the avoidance of conditions that increase intra abdominal pressure the obese patient should be reduced in weight and the wearing of corsets and tight belts should be discouraged Special long handled tools may be used for gardening or housework The habit of sleeping in an upright position with pillows should be developed Careful mastication of food and the exclusion of roughage is a reasonable precaution and the oesophagus should be continually bathed in an alkaline fluid by the use of alkali tablets such as nulacin or prodexin which are allowed to dissolve in the mouth Pain from oesophageal spasm can be relieved by drugs of the atropine group given in a dose large enough to cause slight blurring of vision or dryness of the mouth and then reduced slightly The anaemia responds to iron

Achalasia of the Cardia (Cardiospasm)

The probable explanation of this type of intermittent or chronic obstruction at the cardia (*see* Plate 13 1) is a derangement of neuromuscular co ordination of the oesophageal musculature and as its name implies a failure of the cardia to relax The co ordinating mechanism responsible for peristalsis and relaxation of the lower oesophagus during swallowing is Auerbach s plexus and it is claimed that this is degenerated or possibly mal developed in this condition It is interesting that the operation of vagotomy when the vagus nerve has been cut high in the thorax has been followed by a temporary achalasia There is no evidence to suggest spasm at the cardia and bougies can easily be passed into the stomach The appearance of the oesophagus is hypertrophy of the muscular wall and dilatation in the upper part above the obstruction with no obvious thickening of muscle at the cardia Oesophagitis from food stasis is frequent, and this may be followed by fibrous contraction

Symptoms The patient usually in the younger age groups complains of food sticking" and points to the xiphisternal area to indicate the site of obstruction there may be discomfort but no pain It is usual for the food suddenly to pass the cardia when an adequate pressure has been built up by the accumulation of food and fluid above The

such as stomatitis tonsillitis quinsy or tuberculous laryngitis may give dysphagia but the primary disease is usually obvious This also applies to tumours or the numerous conditions in the neck or thorax which by pressure may obstruct the oesophagus—goitres enlarged glands growths of the lung or mediastinum aneurysms etc

Dysphagia may also be a prominent and dangerous symptom of various neurological disorders such as bulbar paralysis myasthenia gravis diphtheritic neuritis and others It is due to involvement of the pharyngeal muscles and a fatal inhalational pneumonia may occur unless feeding through a stomach tube is instigated at once

Oesophagitis

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Chronic oesophagitis is the more common clinical problem It may result from the continued drinking of some *irritating substance like alcohol* the morning vomiting of the alcoholic is usually a regurgitation of a mucous catarrhal fluid which has collected in the oesophagus during the night Other types of oesophagitis are those produced in the lower part of the gullet from the regurgitation of fluids upwards through the cardia The oesophagus is lined by squamous epithelium and is not equipped to withstand the corrosive effects of the gastric and intestinal secretions Normally the cardia is the guardian against regurgitation of gastric contents

It is unusual for reflux to occur in normal people where the anatomy of the cardia is intact and hiatus hernia is the commonest cause of this type of oesophagitis Yet there is little doubt that repeated vomiting from pyloric stenosis or pregnancy may result in similar changes and repeated bathing of the lower oesophagus by gastric juice may take place in conditions where there is increased intra abdominal pressure as in obesity ascites and pregnancy These may be the start of persistent inflammation in the absence of a definite hernia Although heartburn is most often a functional disturbance of the oesophagus the possibility of oesophagitis should always therefore be considered and oesophagoscopy carried out to exclude it if necessary The pathological changes are those of reddening and oedema of the mucosa with superficial ulceration particularly along the crests of the vertical rugae the ulcers may be covered by a grey sloughing membrane which on its removal leaves a bleeding surface In the chronic phase stenosis follows the ulceration Sometimes fibrous strictures without any inflammation are seen suggesting that spontaneous healing can take place Malignant change is thought not to occur

The mechanism of the cardia as a valve is complex There is a weak sphincter formed by the muscle of the lower oesophagus but regurgitation is *mainly prevented* by the acute angle at which the oesophagus enters the stomach Any rise in the intra gastric pressure tends to increase the efficiency of this mechanism (as happens with the entry of the parotid ducts into the mouth) The crura of the diaphragm are important in maintaining the sharp angulation of the lower end of the oesophagus and the fibres of the right crus which twist around the margins of the oesophageal hiatus exert a pinch cock action which is lost when a hernia is present. There are two main groups of hiatus hernia (*see* Fig 13 1) the sliding type which is reducible into

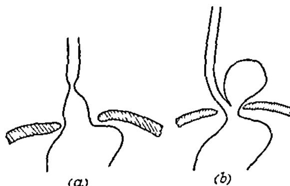


FIG 13 1 HIATUS HERNIA
(*a*) Sliding type (*b*) Paraoesophageal type

the abdomen if not tethered by surrounding adhesions and the *paraoesophageal* or rolling type The essential difference is the angle at which the oesophagus enters the stomach in the sliding type the cardia is patulous and ineffective so that symptoms are frequent in the paraoesophageal one the cardia is frequently still efficient and symptoms are less likely

main a rare disease The skin changes of scleroderma may be associated with similar changes in the viscera Dysphagia is due to an atrophy and sclerosis of the oesophagus which leads to a dilatation and loss of normal peristaltic movements Later there may be a partial obstruction with the development of a chronic oesophagitis

Diverticula

Pressure diverticula are usually pharyngeal and not oesophageal They develop on the posterior wall between the upper and lower divisions of the inferior constrictor where the lumen is narrow with the cricoid cartilage in front The lower division closes the lower end of the pharynx during rest but should relax during deglutition Any pouch formed is enlarged by food and becomes the most direct continuation of the pharynx pushing into the neck They are more common in old age and cause progressive difficulty in swallowing with regurgitation of increasing quantities of food A pouch may be seen and emptied by pressure and is treated by surgery Small diverticula of no clinical significance are seen in the middle third of the oesophagus and are said to be the result of traction on the oesophagus from the scarring of neighbouring disease of the lymphatic glands There seems little evidence for this theory and it is more likely that the protrusions result from dyskinesia of the oesophagus

Rupture of the Oesophagus

Perforation of the oesophagus is a hazard of instrumentation or of swallowing foreign bodies Spontaneous rupture may however occur in a normal oesophagus and creates an emergency that is frequently not considered in the differential diagnosis of acute abdominal or thoracic emergencies and is only discovered at autopsy It is usually a sequel of vomiting and the rupture occurs classically as a knife like slit in the lower third of the oesophagus which is the weakest site when a sudden pressure occurs in the organ The onset is dramatic with excruciating pain in the chest blood staining of the vomit may be seen and a few hours later surgical emphysema may be felt in the base of the neck Rupture often takes place into the pleura giving a pneumothorax containing particles of food or gastric contents Death takes place from a chemical and bacterial mediastinitis unless treated by immediate surgery

Bleeding from the Oesophagus

Peptic ulceration of the oesophagus usually associated with hiatus hernia may result in haematemesis but more often gives chronic bleeding with occult blood present in the stools and is first detected by an iron deficiency anaemia Severe and sudden haematemesis may be due to ruptured oesophageal varicose veins which are a sequence of portal hypertension as in cirrhosis of the liver

The Dyspepsias

Peptic Ulcer

Peptic ulcer of the stomach or duodenum is the commonest organic cause of dyspepsia and its aetiology is unknown Precision in diagnosis may be difficult compared with a disease like malaria and accurate knowledge about geographical incidence is not easily obtained Previously it was thought to be a disorder of civilized races but when it is looked for by careful surveys it is found to be present in primitive Indian races and African negroes so that there is little positive evidence to believe it to be a prerogative of any particular race It occurs in all ages and in both sexes Occasional cases with autopsy are recorded in the literature of the last two centuries and there has been a striking increase in the present century In the First World War peptic ulcer was a very uncommon disorder in the second it was a major problem This increase has been due to the frequency of duodenal and prepyloric ulcers in males Gastric ulcer which previously afflicted the young women of Victorian days is now seen in the older age group with no special sex incidence Duodenal ulcer has occurred in infants it is not uncommon in the late teens and the incidence gradually rises until a peak is reached at 45 or 50 years It is equally distributed among the various occupations and social strata whereas there is evidence that gastric ulcer is more frequent among those with low incomes

Aetiology There is no proof that factors such as infections irregular meals worry tobacco or alcohol play any part in causing the disease though it is possible that they can be important in starting a relapse The stress of modern life often invoked as a cause is a flattering indictment for our civilization but still remains a hypothesis similarly the idea that it occurs mostly in those of a conscientious and dynamic nature who reach positions of responsibility is not supported by statistical surveys Much has been written upon the ulcer personality

patient may notice and describe this sensation and may find trick movements such as increasing the intrathoracic pressure by breath holding in order to start this off Sometimes regurgitation of food is practised to relieve discomfort In later stages the oesophagus may become enormously dilated and mimic a mediastinal tumour or empyema on a plain film of the chest then a spill over of food into the lungs may occur and give attacks of pneumonia

Diagnosis The condition is usually distinguished from carcinoma from the long history The radio logical appearances are characteristic but may be negative in the early intermittent stage the outline of the oesophagus is usually smooth ending with a spindle shaped narrowing at the site of the obstruc tion the barium reaches a height of about 18 cm before it runs through into the stomach the degree of dilatation above mainly depends upon the dura tion of the achalasia Some cases of carcinoma of the lower oesophagus may give somewhate similar smooth radiological appearances at the site of obstruction instead of the expected ragged irregular outline and oesophagoscopy should be performed if there is any doubt

Prognosis and Treatment The attacks are at first transient with long intervals of freedom from trouble No precipitating factors except emotional disturbances have been noted Later in some cases the dysphagia becomes persistent and much discom fort results if the oesophagus is dilated and oeso phagitis develops and progressive loss of weight takes place The most effective treatment is then Heller s operation which consists of an extramucous incision and division of the oesophageal muscles at the cardia In other cases dilatation can be carried out by Negus s bag which is passed so that it lies in the last part of the oesophagus at the level of the cardiac sphincter The bag is then forcibly dilated using water pressure The dilator should be used with radiological control and the stretching should be sufficient to rupture some of the circular fibres of the oesophagus The patient may be relieved by one session though further treatments mav be necessary An older technique valuable in its time but seldom indicated now consists in the use of Hurst s mercury filled bougies which are passed in increas ing sizes The patient is then taught to pass them himself at first before each meal later once a day or less Drug therapy consisting of the use of nitrites such as octyl nitrite inhaled before each meal can be tried in slight cases the effect on relaxing the cardia when seen at X ray may be striking yet it is rarely of practical value Nor do antispasmodics have any effect A half pint of water should be drunk after each meal in order to cleanse the oesophagus and prevent oesophagitis

Spasm of the Oesophagus

Cineradiographic studies of the oesophagus during the swallowing of barium suggest that some cases of otherwise unexplained dysphagia are due to a diffuse spasm affecting the lower oesophagus a condition that sometimes gives curious deformities which have given the descriptive name of cork screw oesophagus It is also claimed that hyper trophy of the oesophageal muscle can be detected on routine radiographs Treatment should be by reassurance and psychotherapy if necessary (as in spasm elsewhere in the alimentary tract) and a trial of anti spasmodic drugs such as atropine or other anti-cholinergic agents

Globus Hystericus

This is often not a true dysphagia but rather a feeling of a lump in the throat usually in the pharynx or upper oesophagus The mechanism may be a type of dyskinesia as in oesophageal spasm It is quite common particularly in women and other nervous symptoms such as feelings of choking or suffocation may be associated with it It usually disappears following explanation and reassurance When the lump in the throat has been present for years as it often has and is associated with other emotional symptoms the diagnosis is obvious When swallowing difficulty is of recent onset globus hystericus should be diagnosed only reluctantly and investigations to exclude cancer or iron deficiency anaemia should always be performed

Plummer Vinson Syndrome

This condition is diagnosed when dysphagia is associated with an iron deficiency anaemia Iron deficiency results in changes in the epithelial tissues such as the finger nails and tongue which are ob vious to inspection and disappear with iron therapy Similar atrophic changes in the pharynx and upper oesophagus are probably responsible for the dys phagia One theory is that there is a disturbance in the normal swallowing reflex resulting in incom plete opening of the sphincter at the pharyngo oesophageal junction Sometimes a curious web formation of the mucosa takes place and can be seen on pharyngoscopy and surgical treatment may be necessary The Plummer Vinson syndrome is practically confined to women and is now rare The difficulty in swallowing is located at the lower pharynx and responds to treatment with iron

Scleroderma

The increasing recognition of the collagen dis eases may result in a more frequent diagnosis of scleroderma of the oesophagus but it will still re

the ulcer to disappear spontaneously flatters the treatment of the moment. Many patients notice that their trouble occurs in the colder months of the year and this is confirmed by statistics which show an increased morbidity from ulcer during the winter. Pregnancy results in cessation of symptoms though they may reappear during the puerperium. Relapses, gradually becoming longer, alternate with shortening periods of remission over 10 or 20 years, so that eventually the trouble is persistent and the usual measures of alkalies and so on are less effective and may suggest the onset of complications such as penetration of the ulcer or pyloric stenosis.

The history varies from this dismal picture to instances where a single episode only of ulcer dyspepsia has occurred in a patient's life or where two or more attacks have taken place at long intervals of time. Unfortunately there is no way of foretelling the future behaviour in any given case so that prognosis is difficult. The threshold of pain differs to a remarkable degree so that a group of patients may present first with a complication such as haematemesis, melaena, anaemia, duodenal stenosis or perforation a deep ulcer crater may have been present for years without symptoms.

There are several associated but non specific symptoms. Heartburn often distressing may be a prominent feature waterbrash is uncommon Nausea and vomiting may be present, but again are relieved usually by bed rest. The vomiting of small amounts of acid gastric juice in uncomplicated peptic ulcer must be distinguished from that seen with gastric stasis. In the latter enormous quantities of gastric contents often without bile may be brought up This story together with evidence that particles of food taken hours or days beforehand are present in the vomit, is pathognomonic of pyloric stenosis. Constipation is often the lot of the ulcer patient and is due to the low roughage diet upon which they often live but must be distinguished from the progressive constipation of obstruction from stenosis

The clinical picture of gastric and duodenal ulcer has been described together because detailed analysis of case histories shows that it is most difficult to separate them although their pathogenesis may be different However there is a tendency for duodenal pain to occur at longer intervals after food and to give the hunger pains so traditionally associated with it. The clinical picture of gastric ulcer is less definite and vomiting is more likely The pain of both ulcers is referred to an ill-defined region across the epigastrium but more on the right in duodenal ulcer Neither ulcers in the stomach nor duodenum undergo malignant change and a small group of patients have both at the same time Hereditary tendencies occur in both, and "ulcer families" are not uncommon it is interesting that the ulcers in these families usually occur at the same site, remaining either strictly gastric or duodenal.

Signs Peptic ulcer is a disease of symptoms and not signs. The most important evidence on clinical examination is to ask the patient to point to the site of pain this is invariably in the upper abdomen and pain occurring below the level of the umbilicus can be excluded as being due to a gastric or duodenal ulcer Palpation usually is negative but with surrounding inflammation or involvement of peritoneum there is deep tenderness and slight guarding of the recti muscles, especially on one side. Rectal examination is also negative but a positive occult blood test on the stool is valuable evidence of an ulcerative lesion of the alimentary tract.

Complications of an ulcer on the contrary result in striking signs which vary from those of a perforation to those of duodenal stenosis, which sometimes gives a succussion splash and visible peristalsis. Time and care are necessary in searching for the diagnostic peristaltic waves which surge from left to right across the upper abdomen The patient must be fully relaxed and the abdomen watched in a good light gentle flicking of the abdominal wall may start the movements. These peristaltic waves are better seen when the abdominal wall is thin and when there is much hypertrophy of the stomach wall from long standing stenosis

Investigations The diagnosis of peptic ulcer depends usually upon the history as clinical examination and radiological investigation may be negative Barium studies should however be done initially in most suspected cases to give objective confirmation to the diagnosis to indicate the site of the ulcer and to exclude complications The specific radiological sign is the presence of an ulcer crater which is usually easily seen in the stomach but may be very difficult to demonstrate in the duodenum When the crater is obvious serial radiology may be used to assess healing Often a barium meal X ray may show non specific features such as pyloric spasm or disturbance of peristalsis Irregularity of the duodenal cap may result from scarring due to an ulcer healed many years previously or from distortion by adjacent structures Such deformities of the duodenal cap taken into account with the history give valuable support to the diagnosis Radiology is of no value in assessing the activity of an ulcer nor is tenderness elicited by the leaden fingers of the radiologist of much significance The emptying time of the stomach may be helpful in the diagnosis of duodenal stenosis where

and a proportion of these patients are of a certain type—restless anxious ambitious and compulsive but not neurotic with the ulcer facies consisting of a tense expression with deep nasolabial folds This personality may however be either the cause or result of chronic dyspepsia with perpetual pain and inability to enjoy the pleasures of eating Only an analysis of successful gastrectomy cases would provide the answer Psychosomatic factors are important in most diseases and are frequent at the onset of such conditions as pulmonary tuberculosis The remarkable influence of emotion upon the alimentary tract where Wolf and Wolff have shown that hostility and resentment can profoundly alter gastric secretion and cause congestion with easy bleeding of the mucosa invites speculation yet there is so far no real evidence that peptic ulcer is a psychosomatic disorder It is perhaps wise to keep an open mind concerning the origin of peptic ulcer and it may be due to some agent not hitherto considered

No one knows how peptic ulcers begin They possibly result from the acute ulcers or erosions—a term used when there is no penetration of the muscularis mucosa—which may occur throughout the stomach It is postulated that those in certain sites fail to heal and leave single chronic ulcers yet the condition of multiple gastric erosions usually known to the clinician as a cause of haemorrhage is often associated with a diminished gastric secretion and gastroscopy shows these ulcers to heal rapidly Again it is possible that some ulcers begin as an inflammation or a focal gastritis or duodenitis and that others especially in elderly people may be of vascular origin from thrombosis in an arterio sclerotic vessel Hormones influence the development of ulcers which are almost unknown in pregnancy but are likely to be activated during corticosteroid therapy Extraneous factors in the food or drink may precipitate some peptic ulcers and it is known that congested mucosa either from psychogenic or other causes is more susceptible to mechanical or chemical trauma Little is known about the factors such as mucus that protect the mucosa from perpetual digestion and ulceration by hydrochloric acid and pepsin It is surprising that ulceration of a mucosa bathed in such powerful corrosive fluids ever heals

Peptic ulcer is a term that includes ulcers occurring in the alimentary tract wherever there is hydrochloric acid and pepsin The various types are oesophageal gastric and duodenal ulcer the ulceration in the small intestine near the site of the anastomoses of partial gastrectomy or gastro jejunostomy and the ulcer seen in a Meckel s diverticulum where there is an aberrant gastric mucosa Such ulcers occur only in the presence of acid and pepsin and have never been described in pernicious anaemia or other conditions associated with achlorhydria when thorough techniques (including stimulation by histamine and perhaps a 24 hr test meal) have confirmed the absence of acid There is no qualitative difference in acid secretion between normal and ulcer patients and certainly no experimental basis for the term hyperacidity There is however a hypersecretion of hydrochloric acid for a given stimulus in duodenal ulcer and the inter digestive secretion is higher than normal particularly at night Whether this is related to the cause or is the effect of ulceration in the duodenum is not known In gastric ulcer the gastric secretion is usually normal or diminished Whenever the hydrochloric acid can be eliminated as by effective surgery or occasionally by X ray therapy the ulcer heals

Clinical Picture There is usually a history of attacks of dyspepsia over a number of years Pain in the upper abdomen is the cardinal symptom This is often described by the patients as aching or gnawing indicating its steady and unvaryin intensity and lasts from short periods to several hours The important evidence pointing to the diagnosis of ulcer is its relation to food It comes on at varying times after a meal and may be precipitated by certain foods such as fats so that the sufferer has himself learnt to avoid such things as fried foods before consulting any doctor The pain is relieved by anything that lowers the acidity of the gastric contents by taking further food or drink alkalies or vomiting A specific symptom of ulcer especially duodenal is the occurrence of spontaneous pain during the night the patient awakes from sleep at about 2 a m goes downstairs and drinks hot milk or takes alkalies returns to bed and resumes sleep with relief of pain The pain of *peptic ulcer is strikingly relieved by* bed rest so that if the symptom persists after 48 hr in bed the diagnosis should be reconsidered or some complication looked for this may be involvement of an adjacent structure such as the pancreas which may give pain in the back a leak into the peritoneum with spontaneous closure or emotional overlay

These bouts of painful dyspepsia last from a week to several months and then for no apparent reason disappear with subsequent complete freedom from trouble and with ability to eat anything There are no proved factors that may start an attack over work worry infections and indiscretions of food or drink are such common features of life that it is difficult to know whether they are coincidental or not in any given case Similarly the tendency for

cantly the consistency of the digested gastric con tents and there is no evidence to support this tra ditional recommendation On theoretical grounds it seems reasonable to avoid stimulants of acid such as strong tea or coffee alcohol on an empty stomach or condiments though there is no clear proof even of the harmful effects of these Otherwise the only dietary advice is that the patient should avoid any particular food that brings on pain

Other drugs used in the treatment of peptic ulcer are belladonna and atropine which paralyse the vagus nerve and may reduce gastric secretion if given in effective dosage The reduction of motility may be useful in the occasional cases where the pain is intermittent suggesting that increased peristalsis is a factor Belladonna in a single large dose up to 7–10 ml (2 or 3 fluid drachms) of the tincture will diminish nocturnal secretion and pre vent night pain It is a good principle to increase the dose to the limits of tolerance as judged by dryness of the mouth or difficulty in accommoda tion and then reduce the dose as necessary Proban thine a ganglion blocking agent, can also be tried but its effects are no better than with belladonna Mental stress is a powerful stimulant of gastric secretion and increases motility of the stomach so that sedatives such as phenobarbitone are often indicated

The chief aim of the medical treatment of the ulcer patient is to relieve pain and allow a normal life to be lived in spite of an ulcer an achievement that is possible in most cases Additional hardships and restrictions from well meaning doctors should be avoided as it may be that the end result of present day medical treatment differs little from the natural history of the disease The only thing that has been proved by a controlled series of cases to increase the rate of healing of an ulcer is bed rest this conforms with the general principle that rest of an injured tissue favourably influences its healing

Surgery The results of surgery are good and can be assessed from many excellent follow up series The mortality rate of major surgery in the hands of experienced surgeons may be 2 per cent or less and is hardly more dangerous to the patient than the inevitable hazards of a chronic ulcer treated medically Controversy still exists concerning the type of operation and at present the choice is between partial gastrectomy with removal of seven eighths of the stomach and gastrojejunostomy with vagotomy vagotomy alone has been abandoned because the secretory and motor effects are rarely permanent and ulcer symptoms return in a high proportion of cases while there are also symptoms due to impaired emptying of the stomach and gastric retention Partial gastrectomy is in favour at pre sent as the most satisfactory procedure follow up results depend upon the individual observer and preferably should be carried out by someone other than the surgeon concerned However even with strict criteria two thirds have complete freedom from symptoms compared with one half of the gastrojejunostomy patients and the chance of stomal ulceration is also less Gastrojejunostomy either with or without vagotomy has a lower opera tive risk and a lower incidence of untoward nutri tional effects afterwards

Indications for Surgery 1 Chronic peptic ulcer uncontrolled by medical treatment The time at which surgery is considered depends upon the amount of disability One should be cautious in advising surgery without a 5 years history Those with a long history of troublesome dyspepsia are more likely to appreciate the alimentary tranquil lity which usually follows it and less likely to be concerned by minor post gastrectomy symptoms The operation is not a necessity and should be undertaken with the full and complete acquiescence of the patient.

2 Gastric ulcer where there is any suspicion of malignancy

3 Where complications such as perforation stenosis or haemorrhage have occurred Urgent surgery may be needed at the time of the haemor rhage or in an interval period when recurrent haemorrhage is taking place

4 In many cases of stomal ulcer as they may be very resistant to healing

Contraindications to Surgery 1 Neurotic patients where a proportion of symptoms are emotional and not due to the ulcer as these may not be relieved by surgery Such patients are very difficult to assess and surgery must not be undertaken lightly Some where the nervous symptoms are a not unnatural consequence of such a tiresome organic disease ob- tain an excellent result others suffer from disabling post gastrectomy symptoms and become gastric cripples Unfortunately it is often impossible to dis tinguish these two groups It is a consolation that ulcer patients as a group do not show neurotic traits

2 The presence of associated disease which un duly increases the risk of surgery With modern anaesthesia and surgical techniques these cases are diminishing

Sequelae of Surgery Dyspepsia following gastric surgery is most likely due to a stomal ulcer though the possibility of its being due to the original ulcer if it was not removed or to other conditions must be considered. These ulcers occur after any anasto- mosis and begin either at the suture line or at a short distance down the efferent loop of the jejunum.

barium is still present in the stomach 6 hours after ingestion and may remain there for days afterwards Radiology may be helpful in the separation of malignant from benign gastric ulcers size alone may indicate malignancy but large ulcers may be simple and heal satisfactorily *the shape is often* more significant particularly with great depth and rolled edges Such lesions usually increase in size with time Malignant ulcers are often situated elsewhere than on the lesser curvature

The fractional test meal often gives a high rising curve in duodenal ulcer due either to rapid emptying of the stomach or increased *secretion of hydro*chloric acid It is an unnecessary test and of little value in most cases Where the diagnosis is suspect the demonstration of achlorhydria particularly if unresponsive to histamine will almost certainly exclude peptic ulcer The fractional test meal is useful in finding evidence of pyloric stenosis the charcoal taken the night previously is present in the fasting juice which is large in amount and may change little at the end of the meal

The finding of an iron deficient anaemia due to *unsuspected alimentary bleeding* is not uncommon and occult blood tests on the stools may be positive but usually become negative after bed rest

Gastroscopy plays little part in the routine diagnosis of peptic ulcer It is impossible to see the duodenum and often difficult to inspect the pyloric canal accurately gastric ulcers can be seen well and *malignant features may be noted and some feel* that it is justified to assess the healing of benign ulcers by this method Unfortunately there are blind areas of the stomach particularly in the fundus so that gastroscopy can never exclude an ulcer

Some patients with ulcer give a long history of incapacitating dyspepsia yet examination and all forms of investigation are negative It seems reasonable then to regard laparotomy with its present low mortality rate as a form of investigation and method of direct inspection of the abdominal con*tents*

Treatment The fluctuating course of the disorder with the sudden spontaneous disappearance of attacks makes it difficult to assess the value of any therapy It is difficult also to tell whether the restrictions imposed upon these patients benefit them or are a needless imposition Treatments come and go and the dyspeptic seizes upon them in his quest for alimentary tranquillity Even traditional methods of diet and alkalies are now open to doubt when exposed to the ruthless but scientific method *of controlled experiment*

The fact that hydrochloric acid is an indisputable necessity in the production of peptic ulcer has led to numerous studies concerning the best method of neutralizing it It is however impossible to neutralize the acid effectively during the day let alone the night An oral dose of an alkali reduces the gastric pH temporarily and relieves pain but the acid rises again shortly perhaps due to the gastric emptying *The main value of alkali therapy is to relieve pain* and it is a fallacy to believe that it influences acidity to any effective degree Sodium bicarbonate is an old time remedy and the acid rebound idea and the danger of alkalosis which caused it to be in disrepute have been shown to be much exaggerated providing the fluid intake is good and the *kidneys normal It is wiser to use the insoluble* alkalies such as magnesium trisilicate or aluminium hydroxide Calcium carbonate is also an excellent alkali The dose of all these is about 4 g (1 drachm) and they can be given as frequently as at hourly intervals if the pain is severe Magnesium oxide can be added to relieve constipation Recently tablets consisting *of alkalies together* with a dried milk preparation have been made of a particular shape so that they can be sucked continuously in the mouth Provided these are sucked at a certain speed such as 3 per hour neutralization of acid *is better* than by swallowed tablets which may pass rapidly into the intestine Perhaps the best but most laborious method of neutralizing the hydrochloric acid effectively is by a continuous milk drip using a Ryle s gastric tube passed preferably through the nose Two or three litres of citrated milk in 24 hr *are given and 2 or 3 meals* a day can be given in addition to the drip It is mainly used when intractable pain is unrelieved by bed rest frequent food and alkalies and may be continued for 2 or 3 weeks the tube usually being changed *each day* There is yet no definite evidence that this more complete method of neutralizing acidity actually quickens the rate of healing It is too early to know the value of ion exchange resins in controlling acidity Rearrangement of meals will modify the behaviour of the pain which often comes on with *clockwork regularity Frequent* eating is effective in relieving pain milk is satisfactory both for neutralization of acid and for its food value particularly in gastric ulcer where under nutrition may play a part and it can be taken in the intervals between meals It is doubtful whether there is any place for the very rigid diets of the past as there is evidence that they in no way hasten the healing of an ulcer compared with ordinary meals Oft n *the* patients are cautioned against many foods without being given positive advice as to what to eat so that they starve for many hours of the day The avoidance of rough particles in the diet may be of importance in gastric ulcers which mostly occur on the gastric pathway but is hardly likely to alter signifi

troubles nor are the victims awakened from sleep because of pain more often they are unable to go to sleep because of their troubled minds The appetite may be good yet a feeling of satiety may develop soon after a few mouthfuls so that the meal has to be discontinued Intolerance to fats is not a marked feature unless they have been advised by their medical attendant to avoid them usually they become very introspective about eating and find that various and in some cases every type of food and drink causes trouble such as discomfort pain and wind Vomiting can be a prominent feature and may continue for years without loss of weight indeed the patients often appear remarkably robust in spite of it

Diagnosis This is suggested when the main complaint is not of pain as in peptic ulcer and by the personality of the patient which is often of a highly strung and nervous type with numerous anxiety symptoms such as weakness irritability loss of sense of well being depression and so on The ulcer patient is not usually neurotic unless made so by his complaint Although the diagnosis of nervous dyspepsia can confidently be made from the symptoms the possibility that some relevant organic lesion may also be present should always be remembered Appropriate investigations to identify or exclude organic disease should therefore be performed and these are particularly important when there has been a recent change in the symptoms

Treatment An adequate history complete examination and thorough investigations will gain the confidence of the patient in his physician so that the best effect of reassurance can be obtained It is wise to avoid telling the patient that nothing is wrong and so giving the impression that the symptoms which are very real are thought to be imaginary The effect of the mind upon the gastro intestinal tract should be discussed with suitable illustrations and the occurrence of pain can be explained by a disturbance of motility giving muscle spasm or some such suitable analogy The fear of cancer so often present should be relieved and faulty ideas concerning the physiology of digestion must be corrected For example the feeling that certain foods cannot be digested is an illusion as sampling by a stomach tube would show the effects from the normal digestive juices with digestion proceeding as expected similarly much worry is caused by wind which is thought to be the result of unnatural fermenting processes going on in the abdomen and much relief of mind may result when the patient realizes that most of the so called wind is in fact swallowed air This aerophagy may be due to the nervous habit of swallowing when the mouth is empty which is frequently obvious during physical examination some object a cork or cigarette holder placed between the teeth will prevent air swallowing and efforts at belching which may further increase the amount of intra abdominal air should be discouraged It is best to prescribe a normal diet with confidence but some have faith in some particular dietetic fads or digestive medicines and efforts to wean them from these ideas may hardly be worthwhile As with all neuroses a careful search for some cause such as domestic upset or additional business stress should be made and may indeed have already been discovered by the patient and recognition of this may hasten cure Medicines either placebos or antispasmodics such as tincture of belladonna in adequate doses or probanthine may give symptomatic relief

Prognosis It is likely that many cases of nervous dyspepsia if diagnosed early can be cured without difficulty Some spend their lives with a sensitive stomach that gives symptoms following either trivial or serious mental stress Where the diagnosis has been missed the patient may have gone from doctor to doctor being labelled as visceroptosis adhesions chronic appendicitis or chronic cholecystitis gastritis and so on These present pathetic pictures with their battle scarred abdomens where numerous viscera have been unavailingly removed Their original symptoms still remain and at this stage are often incurable

Chronic Cholecystitis

Gall stones which are almost invariably associated with inflammatory changes in the walls of the gall bladder occur in 5–10 per cent of the population and are particularly seen in middle aged obese women The specific disease syndromes that they produce are gall stone colic and acute cholecystitis—both dramatic and easily recognized clinical entities The role of chronic gall bladder disease as a cause of dyspepsia is less clearly defined for gall stones are not an uncommon coincidental finding in otherwise healthy people or at autopsy in both cases having caused no symptoms whatsoever Dyspepsia is not uncommon in the same age group as women with gall stones and may be due to hiatus hernia or occur without any structural disease The tendency in the past has been to incriminate any gall stone as the cause of this dyspepsia but a more cautious approach should now be taken in view of the considerable percentage of patients who complain of precisely the same symptoms after removal of the gall bladder the commonest cause of this so-called post cholecystectomy syndrome is an erroneous diagnosis and a search for the real diagnosis should be

The risk is up to 20 per cent of the cases and is more common after gastrojejunostomy or inadequate gastric resections It is mostly seen in young men and more often with duodenal than with gastric ulcer pyloric stenosis gives no immunity The pain is more in the left abdomen and extends below the level of the umbilicus in contrast to gastric or duodenal ulcer Diagnosis is difficult as barium studies frequently fail to demonstrate the crater and gastroscopy is of little value as the beginning of the jejunum cannot be seen occult blood tests are frequently positive as these ulcers are liable to ooze blood If there is no response to medical treatment with rest in bed surgery will be advised a further resection is preferable but vagotomy also gives satisfactory results Stomal ulcers may perforate or penetrate surrounding structures giving a gastrojejunocolic fistula this results in a fatty diarrhoea due perhaps to bacterial contamination of the small intestine and is better detected by a barium enema rather than by a pro gress meal

Failure to gain weight after gastric surgery is common and usually of no serious significance apart from unnecessary worry to the patient It is often associated with steatorrhoea the cause of which may be the rapid passage of the food through the absorptive area of the small intestine or the failure of the food to mix adequately with the bile which is injected into the afferent loop separately There is no contra indication to increasing the fat content of the diet and there is some evidence that it is better to give it at frequent intervals it would be reasonable to assume this to be correct if the above theories of the cause of the steatorrhoea were the true explanation Otherwise it is only usually necessary to explain the mechanism and reassure the patient There is however some indication that pulmonary tuberculosis is more common in gas trectomized patients perhaps due to reactivation of an old lesion and this must be considered as one cause of weight loss though a rare one Anaemia is another complication of gastric surgery and is mostly of the iron deficient type it can probably be prevented in men where there is no method of excreting iron by making certain that any iron deficiency has been replenished immediately after the operation in women the diminished absorption of iron may not keep pace with the loss at the periods in other cases it is the first sign of a stomal ulcer It usually responds to oral iron but intra muscular iron may be needed in some instances Macrocytic anaemia due to deficiency of B_{12} or folic acid occurs rarely

The term dumping syndrome refers to certain vague symptoms that occasionally occur after eating such as fullness faintness and nausea These occur more frequently after the Polya type of partial gastrectomy where the food passes straight into the small gut than after the Billroth I operation where the continuity of the duodenum is main tained The sensations may originate from sudden distension of the jejunum Usually all that is needed is an explanation to the patient with reassurance

Hiatus Hernia (see p 176)

Hiatus hernia is a frequent cause of dyspepsia but the true incidence is difficult to assess as the diagnosis depends upon a complete barium X ray study of the stomach with the patient tilted head downwards to examine the region of the cardia a practice that has not been a routine until recent years Autopsy material is of little value unless special methods of evisceration are practised Most recent knowledge has resulted from the experience of surgeons operating upon the condition The specific symptoms of hiatus hernia is postural heartburn on bending or lying down to sleep at night. Otherwise the symptoms are similar to an ulcer of the stomach or duodenum which is not surprising as their origin is in a peptic oesophagitis often with a definite ulcer of the lower oesophagus

Nervous Dyspepsia

The abdomen is a common site for functional dis turbances where the emotional conflicts of the psyche may cause pain upsets of digestion" and numerous other symptoms They may indeed so mimic the pattern of organic disease that useless operations upon normal organs are performed events which may by their power of suggestion cure the nervous disorder but more frequently pro long any neurosis The gastro intestinal tract has been shown by the experimental studies of Wolf and Wolff to undergo changes in secretion motility and blood flow that reflect the attitude of mind of its owner and in some people symptoms such as anorexia nausea and vomiting and diarrhoea merely symbolize emotions such as sadness disgust, and anxiety and do not indicate disease

Symptoms The symptoms may be localized to the abdomen but frequently are only an incident occurring upon a background of numerous other complaints in various parts of the body The history is often vague with ill defined symptoms such as wind discomfort burning sensations nausea in ability to bear clothes touching the skin liverish ness and so on Pain if present at all may not be sharply localized to the upper abdomen nor have the regularity of ulcer disease and relief by eating or alkalies The attacks are not usually phasic with intervals of complete freedom from digestive

2 *Secondary* There are several explanations of the repeated swallowing that results in the distension of the stomach by air Excessive saliva may be produced by some irritating lesion in the mouth such as dental sepsis or ill fitting dentures or septic conditions of the nasopharynx and catarrh Discomfort in the chest from oesophagitis or angina or in the abdomen from peptic ulcer or gastric neoplasm may initiate efforts at bringing up wind which may cause aerophagy Aerophagy is also common after abdominal operations when there may be several factors present soreness of the mouth or throat from tubes used by the anaesthetist the fluid diet consisting of frequent small drinks and the atonic distension of the stomach and intestines from temporary and partial ileus

There are probably unexplained factors in some cases It is remarkable how some patients can retain such large quantities of air as to cause obvious distension of the abdomen and the mechanism of this is unknown Similarly little is known about the absorption of air or exchange of gases in the intestine and some cases with flatulent dyspepsia as in cirrhosis of the liver and cardiac failure may result from faulty absorption of swallowed air The steatorrhoea syndrome where there is defective absorption of food from the small intestine is an example of a distension of the gut from gas partly from food fermentation and partly perhaps from inadequate absorption

Symptoms The diagnosis is probable when repeated swallowing movements affecting the larynx are seen during the interview with the patient and confirmed when reports from belching break the silence of the consulting room The abdominal complaints are usually of fullness in contrast to the pain of the ulcer patient mainly in the epigastrium and left hypochondrium The accumulation of much air in the stomach may push up the diaphragm and cause dyspnoea in those with a poor respiratory or cardiac reserve already Sudden abdominal distension relieved promptly by bringing up wind is almost certainly due to aerophagy The gas expelled in aerophagy is odourless and unlikely to be confused with the foul odour of long standing pyloric stenosis

Diagnosis Diagnosis is incomplete without X ray studies to exclude an associated organic lesion such as a peptic ulcer or hiatus hernia Gall stones if found are probably unconnected with the dyspepsia and if they are removed many patients continue to have similar symptoms afterwards Absolute confirmation of aerophagy can be made during a barium meal X ray when the process of air swallowing and stomach distension can be directly seen

Minor degrees of volvulus of the stomach from kinking or twisting due to pressure from neighbouring viscera such as a distended colon are not uncommon in healthy people They are usually symptomless and should be ignored various descriptive names such as cascade cup and spill or jack knife stomach are given to them Occasionally severe attacks of epigastric pain and distension may occur sufficiently severe to burst abdomens after laparotomy A similar loculated collection of air may occur in para oesophageal hiatus hernia where the thoracic portion of the stomach may undergo acute distension

Hysterical spasm of the diaphragm gives distension of the abdomen that may be severe enough to simulate pregnancy (pseudocyesis) or intestinal obstruction This is rare and there are rapid changes in the size of the abdomen without eructation of wind It disappears under an anaesthetic

Treatment The main therapy is an explanation to the patient of the normal physiology of the stomach in order to correct his faulty erroneous ideas about wind He should be told to stop trying to belch and if this habit has become fixed a cork or empty pipe placed between the teeth will help as swallowing is impossible with the mouth slightly open but it allows any air to come up naturally

Obvious lesions causing the trouble such as irritating organic disorders in the mouth or nasopharynx or causative diseases in the abdomen should be treated Postural changes such as lying on one side or other may be effective with partial volvulus of the stomach but in this as in post operative aerophagy a stomach tube may give immediate relief A carminative peppermint or cinnamon can be prescribed to be taken when gastric discomfort is felt

The Small Intestine

The small intestine is the most important part of the alimentary tract. The pharynx and oesophagus perform mechanical functions in conveying the bolus of food but can be by passed surgically if necessary removal of the major part of the stomach is compatible with good health and this may be possible even with total gastrectomy excision of the whole colon as in ulcerative colitis leaves no disability except an ileostomy and the patients remain perfectly well and in good nutrition Removal of large portions of the small intestine leads to malnutrition and death and when smaller

made However chronic cholecystitis with gall stones may cause pain in the epigastrium or right hypochondrium and food distress and in the absence of any other disease the gall stones should be removed Medical treatment is unsatisfactory antibiotics are necessary in episodes of acute cholecystitis and antispasmodics may be used in controlling pain Some patients notice pain after eating fats probably due to contraction of the diseased gall bladder more often patients develop fat intolerance after being told by their medical advisers to avoid fats There is no rationale for prescribing a low fat diet in the absence of jaundice (where inadequate fat digestion may take place) unless the patient has himself noticed pain or needs to be on a reducing diet

Dyspepsia of Unknown Origin

There are many cases of dyspepsia where accurate diagnosis is impossible There is insufficient evidence to label them peptic ulcer nervous dyspepsia or suchlike and their symptoms are non specific All investigations including laparotomy may show no sign of structural disease and one is left with speculation concerning the role of food indiscretions allergy the appendix gastritis and so on These cases should be kept under observation as some may develop more specific features which will identify them as peptic ulcers Others will remain unknown until more precise methods of investigation unravel their aetiology

Gastritis

Gastritis used as a popular term to explain otherwise unexplainable dyspepsia should not be confused with gastritis used in its proper pathological sense for there is usually no association between the two Knowledge concerning inflammatory and other changes in the gastric mucosa is obtained from examination of specimens removed at operation autopsy material if the stomach is fixed immediately and specimens removed through the Wood gastric biopsy tube It is then found that chronic gastritis where the gastric mucosa is infiltrated with inflammatory cells is a very common condition is often quiescent and increases with age It results in achlorhydria and is symptomless The lesion of the gastric mucosa which is specific for pernicious anaemia is more an atrophy than an inflammation though it is not always easy to distinguish the appearances from chronic gastritis by the histology of gastric biopsy specimens From the clinical and diagnostic aspects the problem is to correlate symptoms with the histology of the gastric mucosa Beaumont in his direct observations on the mucosa of the stomach of his servant Alexis St Martin through the fistula produced by a gunshot wound first pointed out that dramatic and intense changes could be produced in the mucosa without giving any symptoms whatsoever and this observation has been repeatedly confirmed Acute gastritis due to chemical irritants or alcohol may give no pain or dyspepsia and when most severe result only in nausea heartburn and vomiting It is possible that a gastritis limited to the pyloric antrum is a pathological entity that gives a syndrome similar to ulcer dyspepsia It is also possible that chronic peptic ulcers are often the legacy of an attack of acute gastritis with multiple ulceration. No connexion exists betwen gastritis and neoplastic changes There is scant pathological justification for the term hypertrophic gastritis often diagnosed radiologically and by gastroscopy as biopsy specimens usually fail to show such gastritis and the large folds of gastric mucosa may be merely a variation of normal depending upon the size of the stomach and other factors occurring at the time of examination The only completely established syndrome is that of acute erosive gastritis as a cause of haematemesis and melaena the gastroscopic evidence of multiple erosions that bleed is exact and their rapid healing can be demonstrated. Nothing otherwise is known about this condition and it may be a cause of dyspepsia but until mo evidence is available the use of the term gastritis as a cause of such gastric symptoms should generally be avoided

Flatulence (Aerophagy)

The wind is one of the commonest gastric symptoms and is usually associated with faulty ideas about the digestion of food Many patients believe that the wind they bring up from the stomach is the result of unpleasant fermenting processes due to the improper digestion of food whereas it is mostly swallowed air with an insignificant contribution from fermentation Any discomfort in the abdomen is interpreted by the patient as being due to wind which he imagines he can disperse by eructation As there is really no excess of gas present his efforts only result in the swallowing of air as a swallowing movement usually precedes belching After several attempts have been made without success air being swallowed each time the stomach becomes distended with air which then has to be expelled

Aerophagy can be separated into two types—

1 *Primary* This is a nervous habit that occurs in the absence of organic disease It particularly occurs in neurotic women and there is a background of other emotional symptoms The group accounts for some of the severest examples

2 *Secondary* There are several explanations of the repeated swallowing that results in the distension of the stomach by air Excessive saliva may be produced by some irritating lesion in the mouth such as dental sepsis or ill fitting dentures or septic conditions of the nasopharynx and catarrh Discomfort in the chest from oesophagitis or angina or in the abdomen from peptic ulcer or gastric neoplasm may initiate efforts at bringing up wind which may cause aerophagy Aerophagy is also common after abdominal operations when there may be several factors present soreness of the mouth or throat from tubes used by the anaesthetist the fluid diet consisting of frequent small drinks and the atonic distension of the stomach and intestines from temporary and partial ileus

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lengths are excised the steatorrhoea syndrome with *fatty diarrhoea malnutrition* and vitamin deficiencies results for the small intestine is responsible for most of the digestion and all the absorption of food The glands of the mucous membrane secrete a digestive juice succus entericus which *contains mucin and two enzymes* enterokinase and amylase and the flow of its secretion is stimulated by a meal There are other important enzymes in the mucosa of the intestine which *may* potentiate the activity of pancreatic juice and help to complete *the digestion of food* The main function of the small intestine is the almost complete absorption of the products of food and of other materials such as water salts and vitamins It is probable that the intestinal cell not only performs this function of absorption but also *plays a part in the synthesis* of certain essential substances

The site of the small intestine lying in the middle of the gastro intestinal tract perhaps explains why this organ has been somewhat neglected in the study of abdominal diseases It is not amenable to clinical examination and its distance from the mouth and anus has *so far eluded the endoscopist* Tubes can be passed into it and samples taken of its contents and recently biopsy specimens as well but these methods of study are tedious and usually are re*search procedures Radiology has contributed much and a new impetus has been given to its use* since the use of new and better barium preparations

Methods of Investigation

1 *Inspection of the Stools* Inspection of the stools is a necessity in all cases of diarrhoea whenever any disorder of the small or large intestine is *suspected and indeed in any obscure undiagnosed* illness The diagnosis of coeliac disease idiopathic steatorrhoea or sprue may be obvious from the appearance of a single stool yet defy diagnosis otherwise in spite of numerous and complicated investigations Defective function of the small intestine results in faulty food absorption and the stool *becomes* pale because *of the presence of fat* it is usually foul smelling on account of fermentation of *undigested food products* The *quantity of the stool* is increased because of this failure of absorption both of food and water Microscopy may show fat globules fatty acid crystals and undigested meat fibres

2 *Radiology* It is necessary that frequent films are taken during the barium progress meal such as at half hourly *intervals for* 2–3 hr *or when* indicated *by screening* The rate of passage of the barium through the small *intestine is assessed* although the normal variations are so great—from 1–6 hr to the caecum—that too much reliance must not be placed on this The presence of structural abnormalities like strictures or fistulae may be noted Study of the size of the lumen of the gut and of the mucosal pattern requires the use of special *barium preparations as routine barium sulphate* undergoes physical changes in the steatorrhoea syndrome that obscure the normal feathery pattern of the mucosa These changes result in the flocculation pattern which is a valuable diagnostic sign of idiopathic steatorrhoea and is due to clumping of the barium (*see* Plate 13 2) This is probably due to an *excessive* amount of mucus present *in the gut* and the same curious clotting of the barium can be produced in the test tube wh n a solution of barium sulphate is shaken with fresh mucus Special commercial preparations of barium suspensions such as Raybar *do not flocculate* and allow detailed pictures of the mucosal pattern and bowel outline to be taken (*see* Plate 13.3)

3 *Analysis of Fat Excretion in the Stools* Fat is normally excreted in small quantities such as 2–3 g daily in the stools Part of this comes from the food and part is of endogenous origin from cellular debris Excessive amounts indicate *either* pancreatic insufficiency or defective function of the small intestine All the stools passed by the patient *must be* collected continuously *over* at least a 3-day period and preferably *longer The total fat present* in each *24 hr period is* measured* and on an ordinary diet, should be less than 7 g daily For assessment of the *effect of therapy it may be better to give th* patient a diet of known fat content such as 50 g—the ordinary ward diet usually contains approximately 70 g fat daily Separation of pancreatic disease from the steatorrhoea syndrome usually has to be done on *clinical grounds and* by other investigations (duodenal intubation with estimation of pancreatic enzymes and radiological *studies of the* small intestine) The measurement of split and unsplit fat in the stool is too unreliable for routine use for although fat passed in pancreatic disease should be mainly neutral and unsplit fat it is often altered by *the fat splitting enzymes* of the succus entericus

* A *rapid method of estimating fat in faeces* (as total fatty acids) modified by Dr J M French *from* the technique of Kamer J H van de Huinink H ten Bokkel and Weijers H A (1949) *J Biol Chem* 177 347

A *24-hr* stool collection is emulsified for 2 min *in* a rapid *mechanical mixer* To *avoid frothing* a lid is placed on the surface of the liquid during *operation* A 10-ml *sample of the* measured emulsified faeces (usually 1 000 ml) is transferred by the aid of a syringe into a *150-ml* ground *glass* stoppered conical flask 47 *ml* 5 per cent alcoholic KOH containin 0 4 per cent amyl alcohol are added Boil on a steam bath for 20 min Cool and acidify with aq HCl (about *15 ml* 2 water—1 conc acid) *Add 25 ml* pet *ether shake* well for 1 min *allow to settle and take 5 ml sample of pet* ether layer into a flask Add 2 ml abs alcohol Titrate with N/10 alcoholic soda or tetramethylammonium hydroxide using thymol blue as indicator Calculate total fatty acids as stearic *acid (M Wt 284)*

DISORDERS OF THE SMALL INTESTINE

Idiopathic Steatorrhoea

This is a disorder of the small intestine where no structural abnormalities in the gastro intestinal tract such as fistulae stricture or suchlike can be demonstrated with the naked eye But studies with the jejunal biopsy tube show constant changes in the microscopical appearance of the mucosa The villi are blunted shortened and atrophied The absorptive area must be greatly reduced but it is not known whether this is the cause or the effect of malnutrition Wheat or rye flour is the aetiological agent in most cases as in coeliac disease The offending portion of the flour lies not in the starch but in the protein fraction gluten There is a close resemblance in the clinical pictures of coeliac disease idiopathic steatorrhoea (or non tropical sprue) and tropical sprue patients with sprue usually recover when transferred to temperate climates and the cause of this is probably quite different

Clinical Picture Defective function of the small intestine not only results in fatty diarrhoea but has widespread effects throughout the body from nutritional haematological and electrolytic disturbances The spectrum of symptoms is therefore wide and it is not surprising that it may mimic many diseases and where the diarrhoea is minimal or absent escape detection unless particularly considered Patients may present with three groups of symptoms—

1 *Diarrhoea* The frequency of bowel action may be hardly more than 2 to 3 times daily and be so longstanding that the patient has accepted this as normal so that it is important to enquire specifically about the actual number of bowel actions daily instead of asking whether the bowels are normal There may be episodes of severe diarrhoea with much prostration and bowel evacuations of 3 litres or more of stools The diarrhoea is painless and aggravated by overwork emotion and over indulgence in fats and the pallor of the stools may have been noticed by the patient The bowels may be normal or even costive

2 *General Ill health* Lassitude loss of weight sore tongue and symptoms of anaemia dominate the clinical picture in many patients

3 *Rare Symptoms* Tetany osteoporosis and neurological disorders resembling subacute combined degeneration of the cord sometimes occur

Nothing definite may be found on examination but most patients are undernourished and some are pigmented and of small stature particularly if the condition has existed since childhood The presence of a smooth glazed tongue from glossitis areas of ulceration on the tongue or buccal mucous membrane or angular stomatitis from vitamin deficiencies are frequently present Skin rashes are occasionally seen and may be pellagra The abdomen may be distended and the presence of excess fluid and gas in the small intestine may result in a doughy feel on palpation The blood pressure is often low and dehydration is obvious when the diarrhoea is marked The anaemia is usually macrocytic but sometimes hypochromic Any symptoms depending upon deficiencies of the vitamins of the B complex folic acid B_{12}, D or K or of minerals such as iron and calcium may be seen singly or combined in idiopathic steatorrhoea

Diagnosis This diagnosis should always be considered whenever there is a clinical syndrome consisting of mild chronic ill health subject to relapse and remission recurrent glossitis mild anaemia and variable degrees of intestinal upset Many of these patients are initially labelled colitis nervous diarrhoea lienteric diarrhoea carbohydrate dyspepsia Addison s disease carcinoma of the stomach pernicious anaemia or refractory macrocytic or hypochromic anaemia until inspection and analysis of the stools reveals the true diagnosis

Criteria for the diagnosis of idiopathic steatorrhoea are as follows—

1 A daily excretion of more than 7 g of fat in the stools for 3 or more days

2 The presence of flocculation of routine barium sulphate in the small intestine (*see* p 171) during the first 2 hr after ingestion of the barium and/or wide coils of jejunum or ileum when a non flocculating barium preparation is used (*see* Plate 13.3)

3 Macrocytosis or a macrocytic anaemia occurs in about two thirds of the cases and a full blood count with absolute values of the red blood cells is a useful investigation in all cases of unexplained diarrhoea Macrocytosis is diagnosed when the mean corpuscular volume is above 94 cubic microns Peripheral blood films show macrocytosis with a moderate degree of anisocytosis and conspicuously little poikilocytosis but occasional target cells Occasionally the appearance is indistinguishable from pernicious anaemia A dimorphic picture is seen when iron deficiency is also present A persistently normal blood count is strong evidence against the diagnosis of idiopathic steatorrhoea

Pancreatitis is unlikely to show any radiological changes in the small intestine and the glucose

tolerance test is normal or high but may be low or flat in idiopathic steatorrhoea If facilities are available duodenal intubation with estimation of pancreatic enzymes should be carried out the enzymes are normal in idiopathic steatorrhoea but diminished or absent in pancreatitis

The steatorrhoea syndrome where some or all of the clinical features of idiopathic steatorrhoea may be seen can occur in the following conditions

Crohn s disease stricture or fistula of the small intestine (*see* Plate 13 4) gastro-colic fistula or after gastric operations such as gastro jejunostomy or total gastrectomy so that structural abnormalities of the gastro intestinal tract should always be ex cluded before the diagnosis of idiopathic steatorrhoea is made

Treatment The basic therapy is dietetic Every case of proved idiopathic steatorrhoea should be given a trial on a gluten free diet which may have to be continued for three or more months before *any response is obtained* as there is no means at present of telling which cas s are gluten sensitive The exclusion of wheat and rye flour eliminates bread cake pastry gravy and soups that are thick ened with flour together with buns biscuits and so on These patients only react to the protein in wheat (gluten) and can take wheat starch without harm Gluten is now separated from the wheat on a com mercial basis and the product—pure wheat starch —can readily be obtained The bread though quite palatable is less easy to make than ordinary bread it is more crumbly and heavier because of the lack of the dough making property of gluten The fol lowing instructions and recipes can be issued to the patients—

You may eat a normal diet with the exception of any food made with wheat or rye flour These flours contain a substance which is harmful to you When wheat flour is specially treated to remove the harmful substance the *starch portion is left behind and can be used in cooking* This wheat starch can be obtained from the hospital dispensary and recipes are provided using this to make biscuits loaves and puddings In addition Brown and Polson s or Symmington s corn flour may be used to make puddings custards and sauces and cakes or bis cuits if necessary Soya flour may be used for making biscuits if you find these palatable

You must not have the following Bread biscuits pastry cakes shredded wheat wheat flakes Grape Nuts semolina vermicelli macaroni Ryvita rye bread puddings containing flour or bread custard powder soup gravies or sauces mixed with flour

The following foods may be eaten All meats cheese eggs milk vegetables potatoes rice jam honey jellies For cereals Kellogg s Cornflakes or Rice Krispies or Quick Quaker Oats used for porridge making

You may have any beverages including tea coffee Cadbury s cocoa or drinking chocolate

Ice cream should be made at home as some com mercial brands do contain flour

The following is an example of a wh at flour free diet

Breakfast Kellogg s Cornflakes Rice Krispies o por ridge
Sugar
Cows milk
Boiled or poached egg bacon and tomato
Wheat starch biscuits or soya biscuits or cornflour biscuits or wheat starch loaf

Lunch Average portion of meat, chicken fish.
Spinach cauliflower cabbage or carrots
Potatoes boiled baked or fried
Rice pudding cornflour blancmange junket, jelly Stewed fruit

Tea Milk or tea to drink
Jelly fruit tomato honey jam syrup
Wheat starch biscuits cornflour biscuits wheat starch loaf or cakes (from given recipes)

Supper Milk
Egg custard fruit purée or grated cheese and salad
Wheat starch cornflour or soya biscuits

Gluten free Yeast Loaf

12 oz wheat starch
12 oz lukewarm water and milk mixed
1 oz yeast started with one teaspoonful sugar
½ oz cooking fat
1 teaspoonful salt

Method

1 Add the salt to the wheat starch and rub in the fat
2 Mix the creamed yeast and sugar with the milk and water and stir into the starch thoroughly seeing that no lumps are left
3 Allow the mixture to stand in a warm place for 20 minutes exactly
4 Pour the batter into 2 lb bread tins previously warmed and greased
5 Bake at regulo 5 for 15 minutes then turn up the gas to regulo 7 (400 F) Leave for 5 minutes
6 Take the loaves out of the tins turn upside down on the oven shelf and continue cooking for 15 more minutes

Keeping time About 2 days in an air tight tin

OTHER WHEAT STARCH RECIPES

Wheat Starch Cake

½ lb wheat starch
4 oz sugar
4 oz margarine
1 teaspoonful salt
3 teaspoonfuls baking powder
4 oz milk
1 egg (optional)
Flavour with coconut dates or chocolate

Method Sieve the dry ingredients into a basin rub in the margarine then make a well in the centre and mix enough to make a soft dough Mix quickly and lightly and turn the dough into a well greased shallow tin Bake about 30 minutes in a *hot oven* (400 F) o regulo 7

Biscuits

8 oz wheat starch
4 oz margarine
4 oz castor sugar
1 egg (small)
Grated orange rind or vanilla

Method Cream margarine and sugar add the egg and then the flour Knead lightly to a small ball Roll out thinly prick all over and cut into shapes Place on a greased tin Bake in a moderate oven for 15 minutes Regulo 4 or 250 F

This mixture will make 1 lb biscuits

These biscuits can be made without sugar and may be used with butter or jam etc

Those that fail to respond to the gluten free diet are best treated by a diet high in protein 100–120 g and low in fat 50 g or less Bed rest is indicated when the diarrhoea is severe and this alone often has a striking effect in relieving the diarrhoea Calcium salts have a constipating action and are believed to act by fixing the irritating fatty acids and forming insoluble calcium salts a suitable pre scription is calcium phosphate 2 g calcium lactate 2 g and calcium carbonate 2 g This is prescribed as a powder and 6 g or more is taken three times daily or as often as necessary A troublesome symp tom of vitamin deficiency is the glossitis and the sore tongue usually responds to riboflavin or nico tinic acid The anaemia is corrected by folic acid Vitamin B_{12} or both but many cases still have a slight macrocytic anaemia in spite of this therapy most cases of iron deficiency respond to oral iron but some are refractory to this and require paren teral iron Osteomalacia responds best to large doses of calcium such as 15–30 g of calcium lactate daily and large doses of vitamin D either orally or paren terally—the equivalent of 10 000 units daily at appropriate intervals Cortisone and A C T H may be of value particularly in acute exacerbations and seem to increase fat absorption but do not cure the defect

Although the fat defect usually persists through out life most patients are able to live a normal life provided they are kept under observation to antici pate the development of anaemia and other de ficiency symptoms About 80 per cent respond to the gluten free diet and seem cured provided they avoid gluten Occasional patients die in spite of treatment and death seems to be due to inanition water or electrolytic disturbances such as potassium deficiency or to superadded infection such as tuber culosis

Sprue

This is a disease of the tropics and particularly affects Europeans this may happen after many years in the tropics or sometimes quite soon after arrival Nothing is known concerning its aetiology and gluten sensitivity plays no part The onset is usually insidious and the clinical picture identical with idiopathic steatorrhoea except that megalo blastic anaemia appears more common Cure is usually effected by returning the patient to a tem perate climate Antibiotics are useful in hastening recovery and folic acid is advisable

Other Types of Steatorrhoea

Steatorrhoea secondary to structural defects of the gastro intestinal tract such as gastrectomy gastro jejunostomy gastro colic fistula stricture blind loops or diverticulosis of the small intestine may also give a clinical picture similar to idiopathic steatorrhoea and treatment is along the same lines apart from the fact that gluten plays no part In some of these conditions particularly gastro colic fistula contamination of the intestine by bacteria may be of importance and antibiotics should be used

Non specific Inflammations

Crohn s disease regional ileitis and jejuno ileitis are all conditions in the small intestine showing in flammation of varying degrees and extent This may be diffuse with widespread changes such as oedema and round cell infiltration of the mucosa or local ized as in the classical Crohn s disease where a large mass of granulation tissue simulating tuber culosis appears together with enlarged mesenteric glands Resolution may occur in some cases but the usual event is a chronic fibrosing lesion there is often ulceration of the mucosa with slow per foration and fistula formation into surrounding structures It is not known whether the different clinical types are variants of the same condition nor is anything known concerning their aetiology There are no pathognomonic histological features nor have any organisms been identified

The clinical picture varies from the acute ful minating types of jejuno ileitis to the more usual chronic forms of ileitis involving particularly the region of the terminal ileum Diarrhoea is the pre senting symptom and this is again usually insidious in onset but sooner or later associated with pain the stools have no characteristic features unless the lesion is sufficiently extensive to cause a steator rhoea pus cells and occult blood may or may not be found in them There is loss of weight and in termittent attacks of fever The pain may occur after meals and simulate peptic ulcer Varying degrees of chronic ill health are present and com plications such as intestinal obstruction or fistula formation may often occur fistulae may take place between different loops of gut or into the bladder

Nothing may be found on physical examination but sometimes a large hard perhaps tender mass can be felt in the lower abdomen or right iliac fossa or on rectal examination

Diagnosis may be confirmed by barium X ray

studies (Plate 13 4) but both a progress meal and an enema is often necessary to outline the terminal ileum sufficiently There may be the typical string sign due to long narrowed segment from stenosis and a non flocculating barium is useful in demon strating changes in the mucosal pattern There may be signs of infection such as a raised erythrocyte sedimentation rate and white count

Treatment is conservative unless complications such as obstruction or fistulae arise the results of surgery otherwise are unsatisfactory probably because the lesions are extensive and it is not pos sible by the naked eye to tell their extent and recur rence occurs in a high percentage of cases even when localized lesions are resected There is no specific treatment Plenty of protein is given in the diet as for any chronic wasting disease but otherwise no restriction is necessary unless the diarrhoea is im proved when roughage is removed or the steator rhoea syndrome is present when treatment for this condition is given Antibiotics can be used to counteract infection Results from corticosteroids are disappointing On the whole the illness tends to pursue a slow and benign course

Specific Inflammations

Tuberculosis of the small intestine is often the sequel to the swallowing of tubercle bacilli in an open case of pulmonary tuberculosis There are discrete ulcers more commonly in the ileum that give an intractable diarrhoea this used to be a terminal event in phthisical patients but the outlook has been entirely altered by chemotherapy Rarely there is a localized involvement of the ileocaecal region resulting in a granulomatous mass like Crohn s disease In typhoid fever the small intestine bears the main brunt of the illness and there is ulceration of the Peyer s patches with possibilities of haemorrhage or perforation

Tumours

The small intestine is occasionally the site of benign and rarely of malignant tumours The former tend to occur in younger age groups many types are seen—adenomas lipomas fibromas myomas and vascular tumours Bleeding is probably the commonest symptom of them all and a benign tumour may be the unsuspected cause of a chronic iron deficient anaemia occult blood tests are posi tive Varying degrees of obstructive symptoms from slight colicky attacks to complete obstruction may occur Malignant tumours such as carcinoma may produce a typical syndrome of upper intestinal obstruction with biliary vomiting when they involve the duodeno jejunal junction

Carcinoid tumours also called argentaffin tumours because of their affinity for silver dyes are thought to arise from the chromo argentaffin cells of the normal intestinal mucosa most numerous in the appendix and terminal ileum They are indeed commonest in the ileal caecal region especially the appendix and vary in size from small nodules to large tumours of rubbery consistency with a char acteristic bright yellow colour They may obstruct the lumen of the bowel though most pursue a curi ously benign course even when there are secondary deposits in the abdominal lymph glands or liver others are more rapid in growth Recently it has been shown that carcinoid tumours secrete a vaso motor substance called enteramine or 5 hydroxy tryptamine an indole derivative This substance increases intestinal peristalsis constricts the bronchi and raises the pulmonary arterial pressure and may have caused the pulmonary stenosis that may be a feature of these cases It can be measured in the blood and urine The clinical picture consists of bouts of diarrhoea with cutaneous phenomena such as a reddish blue cyanosis telangiectasis and attacks of flushing with pulmonary stenosis

The Large Intestine

The function of the colon is to dehydrate and store the stools and then eject them at defaecation The caecum and ascending colon seem to act as a reservoir where the chyme from the terminal ileum is solidified by absorption of water salts and glucose This part of the colon seems to remain immobile when studied by X rays and it fills pas sively as a result of activity in the ileum After each meal a gastro colic reflex is set up when the con tents of the colon are driven onwards by a brief powerful peristalsis The faeces then pass into the pelvic colon where they accumulate They do not usually pass beyond the pelvi rectal flexure—the point where the movable pelvic colon joins the fixed rectum at an acute angle The normal rectum is empty except immediately before defaecation The only secretion from the large intestine is mucus which facilitates the passage of faeces The symp toms from the colon are constipation diarrhoea and pain which is referred to the lower abdomen

Clinical Examination

The caecum and d scending colon are palpable in normal people and often the transverse part can be felt in thin subjects The rectum must always be examined in every case where disease of the intestine is suspected and the pelvic colon can some times be felt through its walls If the rectum con tains faeces it should be examined again when empty Any sample of stool remaining on the finger stall of the examining finger must be carefully studied as this alone may allow a diagnosis to be made It should then be rubbed on to a slide and an occult blood test carried out

The Stools Examination of the faeces is an in vestigation of great importance too often omitted and no patient with bowel disturbance has been properly examined until the stools have been in spected Occult blood tests are particularly useful as any ulcerating lesion will give a positive result and malignant disease is readily detected by this simple method which can be done in any doctor s surgery Microscopy of the faeces is invaluable for detecting pus or parasites and bacteriological culture may be necessary when pathogenic organisms are suspected

Endoscopy Proctoscopy is safe and can be car ried out by the inexperienced and enables the anal canal and rectal mucosa to be inspected so that conditions like fissure in ano or ulcerative colitis may be diagnosed Sigmoidoscopy carries a slight risk from perforation of the bowel and should be left to those experienced with the instrument. It is passed with the patent in the knee-elbow position to straighten out the pelvi rectal bend as much as possible and without anaesthetic or other prepara tion Any anaesthetic is an unnecessary hazard and may increase the risk of perforation nor is it needed for biopsy to be carried out Preparation with enemas may give a misleading redness of the rectal mucosa and all that is needed is for the patient to open the bowels if the rectum contains faeces Sigmoidoscopy allows detailed inspection of the entire rectum and often the beginning of the sig moid colon It should never be omitted if a growth of the lower bowel is suspected and can be carried out in out patients

Barium Enema X ray This is a routine method of examining the colon and also the terminal part of the ileum as the barium often flows back past the ileo caecal valve Pictures of the mucosal pattern of the colon can be made after evacuation of the main part of the barium and inflation with air Nevertheless in spite of a perfect radiological tech nique a barium enema X ray is often normal in the early phases of ulcerative colitis and does not ex clude the whole colon being involved by the dis ease nor is it a reliable method of examining the rectum This method of investigation should not be relied upon if negative for a carcinoma particu larly of the caecum and ascending colon can easily be missed

DISORDERS OF THE LARGE INTESTINE

Constipation

Frequency of bowel action in normal healthy people varies so greatly—from twice daily to 2 or 3 times weekly—that definition of constipation is difficult The consistency of the stools is often diag nostic for these are unusually firm and dark from excessive dehydration during their prolonged stay in the large bowel The causes of constipation are as follows—

1 *Physiological* Constipation is a normal ex pected occurrence when the intake of food and fluid is diminished such as may follow abdominal opera tions and during febrile illnesses when diminished food intake is combined with decreased gastro intestinal secretions and motor activity A week or longer may pass without any desire to defaecate and the only precaution necessary is that a finger should be put into the rectum to exclude any unsuspected faecal accumulation in old or debilitated persons

2 *Organic* Constipation is the herald of all kinds of obstruction in the alimentary tract whether in the upper parts from pyloric stenosis or lower down from carcinoma of the colon or a stenosing diverti culitis It is then an ominous symptom and is fol lowed by colic abdominal distension and vomiting

3 *Functional* Most cases of constipation are due to a disturbance of function rather than of structure of the colon Dyschezia is the commonest cause of this type of constipation and results from loss of the conditioned reflex upon which defaecation nor mally depends The sensation from the loaded rectum which is the usual call to stool is ignored so that the rectum normally empty becomes chronically distended with stools and no longer gives the signal for the mass peristalsis of defaeca tion to begin Dyschezia often originates in neglect to respond to the call to defaecate owing to laziness insanitary conditions of the lavatory false modesty or a painful anal fissure It may be precipitated by weakness of the voluntary muscles of defaecation in

the elderly or debilitated and occurs in illness and after operations when the stimulus of the distended rectum passes unnoticed by the patient and is untreated by the nursing staff

Colonic constipation occurs when there is delay in the passage of faeces through the large bowel from deficient motor activity There is no actual weakness of the muscular coat but the reflexes which maintain intestinal activity may be deficient from lack of mechanical stimulation in the food or to some medical disorder such as hypothyroidism

Spastic constipation is a frequent feature of colon neurosis where the colon is irritable and overresponsive to emotional disturbances or to the presence of faeces and results in painful spasms it is also a common symptom of diverticulitis

Symptoms Simple constipation usually gives no symptoms

Patients who are constipated may have symptoms which they wrongly attribute to the constipation These are of a nervous nature and consist of being run down easily fatigued headaches and so on There is a widespread misconception that the traditional daily motion is essential for the maintenance of normal health a belief that is fostered by the advertisers of proprietary purgatives so that many think that missing a bowel movement is of serious consequence The layman is easily convinced of this idea for purges have been considered a panacea for many ills from early times Such a person starts treating himself with cathartics After a thorough evacuation of the entire alimentary tract several days pass before a normal bowel action can again occur The patient now thinks that he is again constipated and continues the use of his favourite remedy Sooner or later his bowel habits become so abnormal that he relies entirely on a daily dose of a purgative for defaecation and the normal stimuli to start off a bowel evacuation such as the regular visit to the toilet a particular meal (often breakfast) or faeces in the rectum are no longer effective This may result in irritable colon (colon spasm colon neurosis) and in extreme cases obsession about the bowels

Simple constipation without cathartic addiction is symptomless except for feelings of distension in the lower abdomen and rectum that may occur in bed patients whose bowel action has previously been normal The idea that absorption of toxins gives symptoms of vague ill health is now obsolete but this might occur when the bowel mucosa is damaged by repeated insults from purgatives Straining at stool from constipation may be dangerous in the patient with cardiac failure or with pulmonary emboli from thrombo phlebitis in the leg and pelvic veins

Diagnosis A careful history establishes the diagnosis of true constipation as distinct from normal variations of bowel action erroneously self-diagnosed as constipation by the patient On examination a colon loaded with faeces may be palpable and a mobile hard mass of stool may simulate a neoplasm but disappears after bowel evacuation. Rectal examination is essential the rectum is normally empty and when it is full of faeces the diagnostic sign of dyschezia it should be felt later when empty to exclude a carcinoma of the rectum or sigmoid colon and sigmoidoscopy carried out if necessary A barium enema is often indicated particularly wh n constipation suddenly develops in a middle aged person to exclude a growth or diverticulitis and it may be necessary in children and younger ages to exclude megacolon A barium progress meal allows the transit time through the colon to be measured Serial occult blood tests should be done when growth is suspected in spite of negative X rays

Treatment No treatment is needed for physiological constipation as the bowel usually regains its normal function spontaneously It may be necessary to initiate this in the bed patient by a saline enema or glycerine suppository or a single dose of a laxative such as magnesium sulphate in the morning Organic forms of constipation are dealt with by treatment directed at the underlying cause

Simple constipation is common and is mostly due to dyschezia or loss of the conditioned reflex responsible for defaecation The first approach is to explain to the patient the normal physiology of the bowels so that misconceptions and alarming ideas can be corrected Reassurance is given that no harm can result from missing bowel actions and that defaecation even once a week can be compatible with normal health The habit of going to the toilet at the same time each day should be restarted even though there is initial failure The lavatory should be warm and the lavatory seat preferably low in order to give a better mechanical action The size of the stools can be increased so that a better stimulus is given to the colon this is done by increasing the fibre or roughage content of the food by the addition of fruit and vegetables bran which is a by product of the milling of wheat contains about 20 per cent indigestible cellulose and therefore is an excellent source of roughage The bulk of the food can be further increased by the following—

Agar This is a dried hydrophilic colloidal substance obtained from various species of algae and is rich in indigestible cellulose When moistened it swells to form a gelatinous mass which acts as an emollient and softens the intestinal contents so adding bulk and keeping the faeces moist It is better

taken shredded or as a coarse not fine powder and can be eaten with other foods or dissolved in hot water and allowed to gel before being swallowed The small amount used in emulsions with liquid paraffin has no therapeutic value and doses of 10–40 g may have to be taken before an effective response.

Psyllium Seeds These tropical seeds contain a large amount of natural mucilage and also swell in the bowel to form an emollient indigestible mass The dose is 4–15 g 1 to 3 times daily and this should be placed on the tongue and washed down with a generous quantity of water "I so gel" is an example of this type of substance

Synthetic Hydrophilic Colloids Methyl cellulose forms a colourless odourless and tasteless stable mucilage—properties which make it useful as a bulk laxative This and other synthetic colloids may eventually replace natural gums and agar as cathartic agents

Liquid Paraffin This oil is a mixture of liquid hydrocarbons obtained from petroleum It lubricates and softens the faecal contents and is indigestible The dose is about 30 ml (1 oz) taken just before retiring or 1 to 3 times daily It is tasteless but many dislike its consistency an objection that can be overcome by the addition of fruit juice or by using emulsified preparations This is of particular value when the faeces must be kept soft following haemorrhoidectomy or when straining at stool must be avoided as in patients with hernia or cardiovascular disease Although liquid paraffin has been used for many years without trouble there are theoretical harmful results as minute quantities are absorbed and it may interfere with absorption of fat soluble vitamins—po sibly important in children —and it may cause lipoid pneumonia if it gains access to the lungs in debilitated or elderly people

Purgatives such as senna aloes or cascara are probably used more than any other class of medical compounds a fact that is not an index of their value but rather a measure of the misconceptions that exist regarding constipation They may with discretion be given in single dosage to initiate defaecation in the bedridden patient but generally the habitual addict to them should be weaned from their use This may be done gradually and glycerine suppositories or simple enemas can be used to stimulate the rectum and initiate the normal conditioned reflex of defaecation A cholinergic drug such as prostigmin can be used to stimulate the contractions of the colon

Megacolon and Hirschsprung s Disease

Both these conditions are examples of gro s constipation occurring in the absence of organic obstruction In each there is enormous dilatation of the colon so that the faecal masses can be felt in the abdomen and large quantities of barium sulphate are needed to outline the colon on an enema X ray In megacolon the rectum is full of stools and a spurious diarrhoea due to retention with overflow may be the presenting symptom. It is thought to follow simple constipation in children but Hurst viewed it as similar to achalasia of the cardia due to a failure of the anal sphincter to relax in the act of defaecation This mechanism is the cause of Hirschsprung s disease where there is a segment of the pelvic colon that fails to relax because of degeneration of Auerbach s plexus here the rectum is empty as the obstruction is higher and good results follow surgical resection of the affected segment. Abdominal pain may occur from partial volvulus of the colon and Hirschsprung s disease may retard growth in children The usual methods for treating constipation are used, and Hurst claimed good results from regular dilatation of the anal sphincter by conical bougies in megacolon

Diverticulosis and Diverticulitis

Diverticula of the colon are usually multiple and are acquired by herniation of the mucosa through the muscle coat of the bowel They are to be seen in the middle aged and elderly The mechanism as with herniation elsewhere is complex and little understood. It is generally agreed that two basic factors are involved pressure within the cavity of the bowel forcing the mucosa against the muscularis and an outlet, or weak point, such as that provided by the gap in the muscle coat due to the entry of blood vessels The unknown factor lies in the behaviour of the plain muscle itself upon which the integrity of the bowel wall depends It has been shown that hypotonia or atrophy of the muscle is not a particular feature of these cases Nor does a positive pressure alone as in acute obstruction produce pouching and it has been suggested that local spasticity of the muscle wall is a more probable forerunner of herniation Whatever the exact mechanism there is no doubt that diverticulosis is a condition of older people being associated with a general loss of elasticity and tendency to hernia formation and is often progressive Diverticulosis is the commonest radiological abnormality of the colon and occurs in about 10 per cent of all colons examined by barium enema X ray The diverticula increase in number and size as the lower end of the pelvic colon is approached but they are very rare in the rectum owing to the thickness of its muscular coat and the support of the surrounding tissues

Clinical Picture Diverticulosis of the colon is a symptomless condition quite compatible with normal health Symptoms occur when inflammation takes place in or around these diverticula resulting in diverticulitis The diagnosis of diverticulitis is difficult to establish exactly as a radiological distinction can often be made in the later stages only when there is thickening and distortion of the bowel from fibrosis The symptoms are often mild and non specific a disturbance of bowel action constipation more commonly than diarrhoea associated with lower and left sided abdominal pain often altered by bowel movements There may be tenderness over the descending colon or in the pelvis where a mass may be felt Low grade pyrexia often occurs These episodes may occur from time to time with normal health between and it is most probable that most cases of diverticulitis pursue a benign course which is controlled by medical treatment Haemorrhage is an occasional symptom Surgery is usually indicated when fibrotic stenosis of the bowel has resulted in a picture identical to carcinoma of the colon or is causing obstruction when there is abscess formation or perforation into the peritoneal cavity or when a fistula has developed either through the abdominal wall or into the bladder

Treatment Many lose their symptoms if a regular bowel action is obtained such as by liquid paraffin or by a hydrophilic colloid like I so gel Much of the pain is produced by spasm and may be relieved by atropine or belladonna pushed to the limits of tolerance or by other anticholinergic drugs In other patients the pain may be continuous and aching from surrounding inflammatory changes a diagnosis confirmed by fever and leucocytosis and an antibiotic such as streptomycin or tetracycline may be indicated It has been customary to prescribe a low roughage diet This may however have little effect upon the condition and only aggravate the constipation

There is no doubt about the indication for surgery when the diagnosis between diverticulitis of the stenosing type and carcinoma is in doubt or with perforation or fistula but these complications are unusual It is not possible to be dogmatic about the necessity for prophylactic resection in chronic diverticulitis with recurrent exacerbations until more facts are known about the natural history of the condition and the prognosis following the use of the modern antibiotics

Ulcerative Colitis

The appearance of the colon in chronic ulcerative colitis is identical to that seen in bacilliary dysentery yet in spite of an extensive search for an organism over many years none has been found and the condition is given the terms "non specific or idiopathic The aetiology is in fact, completely unknown It is a severe inflammatory disorder of part or all of the colon characterized by the rectal discharge of blood mucus and pus with constitutional disturbances such as fever secondary anaemia dehydration and prostration The incidence is greatest between the ages of 20 and 40 years women being affected rather more than men and it has no particular geographical distribution Many hypotheses have been advanced as to its cause an undiscovered virus allergy autodigestion of the mucosa by enzymes such as lysozymes and so on but there is proof of none The latest conception is that it is a stress disorder with changes in the colon brought about by emotional disturbances No one doubts the importance of psychological factors in aggravating the condition and the striking changes both secretory and motor produced in the alimentary tract by emotional disturbances are well established Yet there is no proof of these being the sole aetiological factor in the disease The evidence is more to the contrary Patients with colon neurosis show a strange immunity from developing ulcerative colitis It is true that the victims of ulcerative colitis have in many cases a distinct personality with timidity lack of aggression and over dependence on others they are said by the psychiatrists to be friendly souls but have an undercurrent of resentment frustration and indecision beneath this façade A helpless and despairing frame of mind could well result from the disease and it is interesting that these characteristics often disappear following treatment of the condition by an ileostomy

Clinical Picture The onset is usually insidious the first symptom noticed being the passage of blood and mucus with or without diarrhoea Even in cases which appear to begin acutely a history can often be obtained of slight irregularity of the bowels with occasional blood or mucus over some months or possibly years before the onset of acute symptoms Diarrhoea always develops sooner or later About one fifth start abruptly and are of an acute fulminating type with severe diarrhoea and toxaemia from the beginning The rest of the cases however have repeated attacks over a number of years with long intervals of normal bowel function and some have chronic diarrhoea of varying severity more or less continuously

The diarrhoea may be mild from 3–4 times daily but up to 20 times or more in the acute episodes The stools are liquid as in dysentery or semi solid and contain bright red blood pus and mucus Blood may be passed in large quantities by itself Abdominal discomfort is often but not always pre



Achalasia of the Cardia



Barium Meal Showing Small Intestine Pattern at 1 hr in a Case of Idiopathic Steatorrhoea with Flocculation of the Barium

A simple solution of barium sulphate in water was used The appearance is largely an artifact due to the clumping of the barium probably from excessive mucous secretion

Plate 13 2



BARIUM MEAL AT 1 HR IN THE SAME PATIENT AS PLATE 13 2 USING A NON FLOC CULATING BARIUM PREPARATION (RAYBAR)

The true outline of the intestine can now be seen It is dilated with the folds of the valvulae conniventes showing prominently (ladder appearance)



Narrowed Coils of Ilium from Crohn s Disease

sent Actual pain is rare except immediately before defaecation when colic may occur but this disappears afterwards even if flatus only is expelled Tenesmus occurs if the anal canal becomes involved The abdomen is retracted but otherwise normal Tenderness particularly if severe indicates that the inflammation has spread to the peritoneum and caused local peritonitis There is frequently severe constitutional disturbance with high fever prostration and loss of weight Anaemia dehydration and electrolytic disturbances depend upon the loss of blood in the stools and frequency of diarrhoea

Local complications of the disease consist of strictures which are usually benign but may be neoplastic as between 5–10 per cent of colons involved by ulcerative colitis eventually undergo malignant change Localized abscesses are unusual except in the perianal region where multiple fistulae in ano may develop and recto vaginal fistula is often seen Perforation is a highly dangerous complication and is frequently missed so that the fatal peritonitis is only discovered at autopsy There is usually a history of sudden pain or shock but the physical signs seem to be modified in these extremely debilitated and wasted patients so that abdominal rigidity and even tenderness may be surprisingly slight or even absent In suspected cases a radiograph with the patient sitting up should be taken in order to detect air or gas under the diaphragm Distal complications consist of abscesses skin lesions pyodermia iritis and arthritis

Diagnosis The diagnosis can usually be confirmed by proctoscopy or sigmoidoscopy as the rectum is nearly always involved in ulcerative colitis but the latter should be performed with care as the bowel is friable and easily perforated The early changes are those of hyperaemia and easy bleeding with a granular appearance from distended mucosal glands Superficial areas of ulceration may occur and progress until the whole mucous membrane is shed and there may be gross oedema so that the lumen is almost obliterated Later the rectal wall becomes rigid and does not move easily with air insufflation narrowness with stricture formation and pseudo polyposis is seen in the chronic phases of the disease

The faeces must always be examined for dysentery organisms Pus and red cells are always present Sometimes the stools seem to consist entirely of pus which may be confused with fat if naked eye examination only is carried out

A barium enema X ray carries a risk of perforation during the acute stage and should b deferred until later when the extent of colon involvement can be assessed Loss of haustration so that the colon appears as a rigid tube is the characteristic appearance and pseudo polyposis may be seen The terminal ileum apart from the last 5 or 10 cm is rarely involved but if an ileo colitis is suspected a barium progress meal must be performed and the small intestine function studied by the faecal fat excretion

Treatment Many cases seen by the physician are adequately treated by medical means This particularly applies to the milder cases where only part of the colon is involved such as the rectum and sigmoid colon and to those where attacks may occur with long intervals of slight diarrhoea or normal bowel function The diarrhoea may be alleviated by the insoluble sulphonamides or oral antibiotics which eliminate secondary infection of the inflamed bowel but otherwise do not alter the course of the disease Nutrition should be maintained as far as possible by a high calorie high protein diet the value of eliminating roughage is debatable as many patients are unaffected by it Anaemia from iron deficiency due to blood loss will be corrected by oral iron such as ferrous sulphate or gluconate but in some patients this may increase the diarrhoea and an intramuscular preparation of iron such as imferon (an iron complex with dextran) should be given The anaemia of infection responds only to cure of the disease or blood transfusion Depletions of water salt or potassium may have to be corrected Most important in the treatment of such cases with intermittent or chronic diarrhoea is the handling of the patient with measures to keep up the morale such reassurance as indicated and discussion of emotional difficulties Bed rest often strikingly improves the diarrhoea

The recent improvements in the surgery of ulcerative colitis are such that this should be considered in all severe cases and the best results are obtained when there is complete co operation between the surgeon and physician in treating the patient The introduction into this country of an efficient bag which adheres to the skin has revolutionized ileostomy so that this no longer prevents the patient from living a normal life Since the use of antibiotics total colectomy carries a much lower mortality and is usually performed either at the time of ileostomy or later when the condition of the patient warrants it Colectomy is advisable as the remaining disorganized colon may be a source of infection and can undergo malignant change even though the main stream of bowel contents has been by passed from it Surgery is advised in the following circumstances—

1 If the patient is completely disabled by the disease in spite of medical treatment and after a sufficient duration of time to exclude the possibility of a spontaneous remission taking place

2 When the patient s life is threatened by a relentless progress of the disease This is more likely to occur in the acute fulminating type Most acute episodes and relapses of ulcerative colitis can be controlled by medical treatment and ileostomy should be done during a quiescent phase whenever possible

3 In the presence of complications such as strictures neoplastic change iritis arthritis and so on

The preparation of the patient for ileostomy is important and it should not be done without full co operation The approach should be a gradual one as only in extreme and exceptional cases is it necessary to use the operation as an urgent and life saving measure The patient is introduced to those with ileostomies living a normal life so that the practical problems of ileostomy can be discussed beforehand and the matter carefully considered The ileostomy always has to be permanent but is compatible with normal health unrestricted exercise marriage and the bearing of children

Corticosteroid therapy is effective in the acute attack whether this is the first onslaught of the disease or a relapse as it usually helps to induce a remission It carries the usual dangers of such treatment and should not be continued unnecessarily The dose must be increased for surgery It is useless in the chronic phase and does not prevent relapses

Proctitis

It is possible that proctitis may exist as a separate entity from ulcerative colitis It is difficult to prove this point as many cases of ulcerative colitis may remain confined to the rectum before spreading around to involve the rest of the large bowel and there is no means of distinguishing these In certain patients with proctitis there is a known cause such as the use of wide spectrum oral antibiotics deep X ray therapy or lymphogranuloma venereum

Clinical Picture The passage of blood is the first and sometimes the only symptom This may coincide with periods of constipation and it is likely that the hard stools of constipation may aggravate the bleeding Sometimes there is a true frequency of bowel action but more often the cause of the diarrhoea is the passage of blood and mucus without faeces Pain is usually absent The patient s health and nutrition remain good in contrast to those with ulcerative colitis The disease waxes and wanes over months or years and is more of an inconvenience than a disability Many probably subside spontaneously Stricture formation may occur but it is not known whether there is danger of malignant change

Diagnosis Proctitis is diagnosed and carcinoma of the rectum excluded by the appearance of the rectal mucosa through the proctoscope the changes of hyperaemia and granularity are similar to those seen in the early stage of ulcerative colitis A barium enema X ray is necessary to exclude changes in the colon The descending and sigmoid colon are however frequently ahaustral and narrow in normal people and this without alteration in the mucosal pattern does not indicate any extension of the disease

Treatment Reassurance and a simple explanation together with a warning that the condition may persist often allows the patient to live a normal life Hardened stools should be lubricated and softened with liquid paraffin The haemoglobin should be checked to anticipate any anaemia from blood loss Insoluble sulphonamides are valuable in the treatment of secondary infection of the inflamed and oedematous mucosa Hydrocortisone suppositories (50 units of hydrocortisone in 1 g cocoa butter) or enemas (50–100 units of hydrocortisone hemi succinate in 100 ml saline) may be used and may reduce the bleeding strikingly or induce a remission

Ileocolitis

This is a rare condition involving the ileum and proximal colon giving severe diarrhoea that may be fatal The bowel shows non specific inflammatory changes The importance of it is that it must be distinguished from ulcerative colitis as ileostomy in ileocolitis is contra indicated This distinction may be made by sigmoidoscopy as the rectum is normal in the early stages by a barium progress meal showing ileal disease and by an abnormal fat excretion in the stools If progress is progressively downhill in spite of treatment steroid drugs should be tried Other forms of colitis such as regional colitis probably allied to Crohn s disease may occasionally be seen

Tumours of the Colon

Adenomas are the commonest benign tumours and are polypoid They may occur singly and result in bleeding with or without cramp like pains in the lower abdomen They are potentially malignant and removal should always be considered They can be seen in the rectum but are otherwise visualized radiologically using a double-contrast technique by the introduction of a radio opaque medium and air to outline the mucosal pattern

Multiple polyposis of the colon is a familial and pre malignant condition It gives rise to haemorrhage and diarrhoea from secondary infection Colectomy should be performed This condition must be distinguished from the pseudo polyposis of the healing phase of ulcerative colitis this is due

to an excessive regeneration of epithelium and does not undergo neoplastic change

(For carcinoma of the colon *see* p 201)

Irritable Colon (Colon Spasm or Colon Neurosis)

This is one of the commonest functional disorders of the gastro intestinal tract giving rise to symptoms of colonic disease from disturbance of bowel function rather than of structure of the large bowel The aetiology of most cases is entirely psychogenic It has been shown experimentally that changes in the colon such as contractions hyperaemia and increased mucus secretion result from emotional reactions and the intensity of these is directly re lated to the degree of colonic change The reason why the colon rather than other organs bears the brunt of mental conflict in certain people is un known Some have sensitized their colons by habitual purgatives Occasionally irritable colon may follow dysentery Mucomembranous colitis a variation of this syndrome where excessive mucus secretion causes mucus casts to be passed is now disappearing

Symptoms The leading complaint is usually of discomfort and pain in the lower abdomen The pain is usually a dull continuous ache sometimes gnaw ing or like a toothache but the intensity may sometimes be severe and simulate a major colic Alteration of the pain by defaecation confirms its colonic origin

The condition is not infrequent in intelligent and conscientious people otherwise healthy and free from neurotic traits In others irritable colon occurs on a background of nervous symptoms These patients are usually bowel conscious and com plain of constipation meaning that it is necessary to take a purgative or enema in order to obtain a bowel movement On enquiry as to how long the patient goes without a bowel action the typical reply is I never let my bowels go more than a day without a movement They believe they are con stipated but really maintain a state of diarrhoea Similarly they may be dissatisfied with the amount or consistency of their stools lamenting that their bowels do not move enough Extreme examples occur when a bowel obsession results in the patient s whole life being centred around his bowel action and faeces

Diagnosis Organic disease such as growth or diverticulitis each of which can give identical symptoms must be excluded The stools in irritable colon may be narrow and ribbon like but this is a variable feature as the spasm causing it is inter mittent The barium enema X ray is usually normal but areas of painful spasm may appear during the screening and this may also be seen during sigmoidoscopy

Treatment These patients are often fearful of organic disease and many have cancerophobia Reassurance and an explanation of the mechanism of the symptoms may result in alleviation or cure Correction of faulty physiological ideas about con stipation (*see* p 193) and the violence of purgatives is essential Antispasmodic drugs such as bella donna probanthine or nitroglycerine may be effective A normal diet is allowed except where definite evidence exists that certain articles of food cause the pain It must however be remembered that the seat of the trouble lies not in the bowel but in the patient s conflict with his environment and emotional difficulties should always be dis cussed with the patients Many patients recover with this therapy or are able to ignore their pain A small group become chronic sufferers and are a burden to themselves and their doctors

Malignant Diseases of the Alimentary Tract

Malignant disease of the alimentary tract is a common hazard of the middle aged and elderly patient and accounts for a majority of all cancer deaths Hope of survival lies in surgery except in the tongue where the lesion being visible is detected at an earlier stage and is treated by irradiation The chance of complete removal of growths is improved by early diagnosis This is most difficult because there frequently are no early symptoms or signs of gastro intestinal cancer The first complaints of the patient are often due to disturbed function of the stomach or colon—vague indigestion or disturb ance of bowel action such symptoms are often treated for long periods before the serious nature of the trouble is realized This may be because the image that many doctors have in their mind of such growths is of a patient who looks ill has lost weight and shows definite abnormal physical signs of a lump or enlarged liver The conception that students should have of early growths is of a healthy middle aged person with vague symptoms of gastro intestinal origin and with no physical signs no such person should be treated for longer than a month without measures being taken to exclude neoplasm The prognosis is often worse when the patient is young and can be to some extent correlated with

the histological differentiation of the growth being worse when the cells are anaplastic and better when a highly organized structure such as an adeno carcinoma is present—thus being similar to such growths elsewhere in the body One might think that the outlook would be improved when the lesion presented at a narrow part of the alimentary tract such as the cardia pylorus or descending colon for obstructive symptoms would lead to early detection This is true to some extent yet this early diagnosis may be obviated by early dissemination of the growth In the larger reaches of the gut such as the stomach or caecum growths can reach a great size before disturbing the function of the organ They may then present as an anaemia of the typical iron deficient type due to loss of small but continued amounts of blood in the stools Every effort should be made to find the cause of such anaemia before it is treated Other varieties of anaemia may also be present the anaemia of in fection because of chronic infection of the ulcerated surface or the anaemia of malignant disease Both of these are normochromic and normocytic and respond to nothing except cure of the original con dition or temporarily to blood transfusion The tendency of gastro intestinal growths is to ulcerate and bleed this bleeding may be severe enough to result in haematemesis or melaena but is more frequently unnoticed by the patient It is however easily detected by the occult blood test on the stools this is a test that can be done by any prac titioner in his surgery and recent analyses have confirmed its accuracy It is probably positive in over 90 per cent of neoplasms A series of three negative occult blood tests is good evidence of the absence of a growth in the alimentary tract It is particularly useful when the history suggests neo plasm in spite of negative X rays of the entire gut The finding of persistently positive occult blood tests is then enough evidence to advise a lapar otomy

Carcinoma of the Tongue

Carcinoma of the tongue is one of the few growths that is decreasing in frequency It starts usually as a small firm lump at the edge of the tongue and then ulcerates often showing the firm indurated and rolled margin that is characteristic of malignant ulcers It should be a rule that any such single ulcer which fails to heal in one month should be con sidered as possibly malignant until proved otherwise by microscopy The pathology is that of a squamous carcinoma The tongue is a site where radiation treatment of cancer is more successful than surgery both in giving relief of symptoms to the advanced case and in the treatment of the early lesion

Carcinoma of the Oesophagus

Carcinoma of the oesophagus affects males more than females and presents at a later age than other cancers It is most common in the lower third becoming progressively less common in the upper part The predominant presenting symptom is dysphagia of short duration although occasionally cases have had some difficulty in swallowing for many years previously This involves first solids then liquids It is painless at the beginning then gives substernal discomfort, and finally a pain which may be continuous and severe The patient can locate the site of obstruction fairly accurately in many cases As the stenosis increases so the food regurgitates the late stage is complete oesophageal obstruction with death from starvation Radiology is accurate in this diagnosis and an irregular stric ture is commonly seen A direct view of the lesion can easily be obtained by endoscopy and complete confirmation had by biopsy The pathology is that of a squamous carcinoma unless in the distal oeso phagus when an adenocarcinoma of stomach origin is seen Surgery is the first line of therapy Five year follow up results are however poor Radiation is advisable for some cases and careful dilatation of the constricted area by guided bougies prolongs life in some inoperable cases and may avoid the need to extend a miserable life by gastrostomy

Carcinoma of the Stomach

This is a frequent cancer in males between 40 and 60 years and it appears to be on the increase perhaps due to the greater span of life It occurs among all races and in all parts of the world No aetiological factors are known and there is no association with simple gastric ulcer

Pathology The tumour may develop anywhere in the stomach but approximately 50 per cent involve the distal half or third Macroscopically th commonest lesion is an adenocarcinoma which starts as a localized polypoid mass growing into the lumen of the stomach next is the ulcerating cancer often in contrast to benign ulcers growing on the greater curve or in the pyloric canal The rarest is the leather bottle stomach an infiltrating scirrhous lesion where the stomach retains its shape with walls that become thickened and im mobile The clinical picture of carcinoma depends upon the location of the neoplasm its size and ex tent and by its tendency to ulcerate bleed or metastasize

Clinical Picture There are no symptoms or signs of an early growth in the stomach It is perhaps fortunate when the neoplasm occurs at the pylorus (60 per cent of cases) giving the dramatic picture of

pyloric obstruction or at the cardia (8–10 per cent of cases) when the patient presents with more specific symptoms of dysphagia and substernal distress More often the clinical picture is vague with anorexia nausea fullness after eating vomiting and a dyspepsia without the typical pattern of a peptic ulcer The good health of the patient at this stage together with the absence of any abnormal physical signs gives a false sense of security and precious time is lost with symptomatic treatment by diet and alkalies A frank melaena or haematemesis is unusual with cancer of the stomach more often the bleeding is so slow that it passes unrecognized by the victim who goes to his doctor with an iron deficiency anaemia The anaemia may be cured by iron therapy and the patient returns in a few months with carcinomatosis The condition is progressive without remissions

No abnormal findings on physical examination are anticipated in the operable stages While the presence of a palpable lump in the upper abdomen mobile and usually not tender indicates a relatively large sized growth it by no means suggests that it is inoperable but the finding of an enlarged liver ascites or a Virchow s gland behind the inner end of the left (or sometimes right) clavicle is a sign that diagnosis is too late Similarly rectal examination may reveal a mass in the pouch of Douglas or in both ovaries (Krukenberg tumour) and save an unnecessary operation A detailed search must be made for deposits in the body elsewhere

Investigations The accuracy of a barium meal X ray is such that about 90 per cent of growths of the stomach can be detected this way The filling defect is usually unmistakable though sometimes the ulcer cancer can be confused with simple gastric ulcer it is then permissible to X ray the patient again after three weeks on bed rest malignancy is unlikely though not excluded if the crater is smaller *Lesions in the region of the cardia or fundus can* be seen only with a careful examination of the upper third of the stomach with the patient tilted head downwards In certain cases of pyloric obstruction it is impossible before laparotomy to know whether the cause is simple or malignant

If the X ray is negative and cancer is still suspected serial occult blood tests should be done on the stool If these are negative a neoplasm is most unlikely

Other investigations less reliable but often helpful are the fractional test meal which may show traces of blood present or an achlorhydria in two thirds of the cases or gastroscopy where a direct view of the lesion can be obtained The naked eye appearance is however inadequate to determine whether an ulcer is benign or malignant This is difficult when it is handled as well as seen at operation and the microscope is the final court of appeal A search of the gastric contents for malignant cells can be carried out and the chances of a successful find depend upon the enthusiasm and experience of the person looking for them

Prognosis The most important factor in the prognosis is the nature of the lesion and although every effort should be made to diagnose the condition at the earliest possible moment it is usually the invasive and metastasizing properties of the cancer that determine the issue The overall prognosis is really appalling and would seem to be difficult to alter until there is some new and simple test for detecting cancer patients The Americans have tried Mass Barium Meal X rays but this has been found to be impracticable nor would it appeal to the population in this country

Treatment The only hope for the patient with gastric cancer is adequate removal of the lesion This is sometimes possible but more often a palliative operation is carried out particularly in the presence of obstruction The follow up figures compare favourably with more radical operations and the present tendency is to avoid total gastrectomy with its incapacitating sequelae of nutritional disturbances

Carcinoma of the Large Bowel

This is a frequent tumour accounting for about 15 per cent of all tumours It affects a similar age group to those with lesions in the stomach but is only slightly more common in men The outlook is better than from any other part of the gastro intestinal tract There are no known aetiological factors in the usual case where it occurs in otherwise healthy people However there are two definite precursor lesions—ulcerative colitis and congenital polyposis of the colon

Clinical Picture *The first symptoms are a dis*turbance of function of the colon with varying degrees of constipation or diarrhoea either singly or alternating Thus the presence of a growth should always be suspected in any middle aged person with a change of bowel action particularly when previously regular The clinical picture often varies according to the site of the lesion The scirrhous carcinoma which produces a ring like constriction of the gut is curiously likely to occur in the distal colon where the stools are solid and so gives symptoms of progressive lower intestinal obstruction that start with vague colicky pains and constipation The large fungating adenocarcinoma is more likely to arise in the caecum and ascending colon The contents of the bowel are fluid and it grows to a large

and palpable size without causing any obstruction The surface becomes infected and bleeds easily The bowel disturbances may be quite slight with vague alternating constipation and diarrhoea Sometimes the presenting features may be unassociated with gastro intestinal function and the patients first appear with a severe anaemia or ill health with loss of weight Infection associated with the growth either inside the lumen or on the peritoneal surface may result in pyrexia and simulate appendicitis or regional ileitis

It may be possible to palpate the tumour particularly as much of the large bowel can be felt quite easily There may for example be a fixed mass in the right iliac fossa or a mobile lump in the transverse colon Stools can mimic a neoplastic mass in the colon and sometimes are significant in that their presence is due to a hold up from a small impalpable neoplastic stricture distally Rectal examination is a vital part of the clinical examination of every suspected case and is of supreme importance as the rectum is the commonest site of *growths in the large bowel* and most can be easily felt and diagnosed at an early stage Sigmoidoscopy is essential in visualizing the pelvi rectal junction and pelvic colon which may be difficult to see on the barium enema X ray Carcinoma of the caecum and ascending colon may be better seen on a barium progress meal but can be missed altogether Occult *blood tests are practically always positive and it* must be rare for a growth of the large bowel to exist when a series of three occult blood tests are *negative*

Treatment Many of these growths are amenable to surgical resection and often an end to end anastomosis can be done Otherwise a colostomy is re*quired* Rectal lesions are treated by abdomino perineal resection with colostomy Even if the growth cannot be completely removed life is made far more bearable for the patient who loses the distressing tenesmus and bloody diarrhoea of the rectal growth Growths of the large bowel may remain localized for long periods of time and the prognosis is such that 50 per cent of operable cases are alive at the end of 5 years

Carcinoma of Duodenum and Small Intestine

The small intestine is the least likely site of malignant growths in the alimentary *tract The first part* of the duodenum seems almost immune and it is striking how neoplasms of the pyloric end of the stomach *fail to pass the pylorus* However lesions in the second and *third* part of the duodenum account for the majority *of the* carcinomas of the small intestine and *cause* an *upper* intestinal obstruction that can be *distinguished* from pyloric stenosis by the presence of bile in the vomit. The whole symptomatology of tumours of the small intestine depends upon the gradual and progressive onset of intestinal obstruction, diagnosis being suggested by the colicky nature of the pains Intussusception may give the sudden onset of acute symptoms and is more likely if the tumours simple or benign are attached to a pedicle Barium studies of the small intestine are usually diagnostic but it must be remembered that the ingestion of barium can easily convert a partial obstruction into a complete one and so may be dangerous Carcinoma of the ampulla of Vater gives a typical picture with a painless progressive jaundice which may be distinguished from carcinoma of the pancreas by the presence of occult blood in the stools

Argentaffin carcinomas also called carcinoid tumours because of their occasional benign tendencies occur as bright yellow nodules of a rubbery consistency and have an affinity for silver dyes They are seen in young adults and are common st in the appendix and terminal ileum Interesting *recent developments indicate that they are an* endocrine growth which secrete a hormone—5 hydroxy tryptamine This is a normal secretion of the argentaffin cells of gastro intestinal mucosa but when the levels in the serum are increased as with such a tumour a syndrome may *result that consists* of flushing attacks cyanosis dyspnoea *abdominal pain* and *diarrhoea (apart from the effect of* a tumour) and secondary pulmonary hypertension

Other Tumours

A large number of benign neoplasms have been described as occurring in the alimentary tract *but* these are rare Perhaps most important are the leiomyomas which are most likely in the upper intestinal tract their tendency *to bleed* is great and anaemia of the iron deficient *type is* often the method of onset In contrast to these *benign* lesions are the sarcomas fortunately again rare *The* rate of growth and tendency to metastasize *is* greater than the carcinomas The clinical picture *is* accordingly more acute but the occurrence *of symptoms* depends upon the same *principles as with all* other tumours disturbance of functions *obstruction* if the site is at one of the narrower regions of th gut and varying degrees of haemorrhage

Abdominal Carcinomatosis—the Final Picture

Spread from growths of the stomach intestine and colon occurs via the blood stream so *that* secondary deposits in the liver are a feature of *them* all in fact an enlarged liver may present before any evidence of the primary growth It can be distinguished from cirrhosis of the liver sometimes by

palpation of the firm deposits on its surface but more often by its size which increases Spread also takes place through the lymphatics involving the mesenteric lymph glands and through the lymphatics of the posterior mediastinum the supraclavicular group giving the classical Virchow s gland on the left side Direct invasion is a feature of all such abdominal growths and involvement of the peritoneum results in malignant ascites—an exudate where malignant cells can sometimes be found The clinical picture at this stage is usually one of progressive cachexia—the increasing size of the abdomen contrasting vividly with the wasting of the body elsewhere The care of the dying is one of the most difficult and trying problems for any doctor and is the most severe test for the doctor–patient relationship Pain can be controlled by one of the synthetic analgesic drugs such as pethidine or morphia depending upon the severity of the pain Paracentesis may give relief The anaemia can be treated by iron when intramuscular therapy may be necessary to keep pace with the blood loss from the alimentary tract Chlorpromazine should be given a trial as it can be effective in controlling the vomiting and may bring mental tranquillity

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CHAPTER 14

Diseases of the Biliary System, Liver and Pancreas

C F HAWKINS

The Biliary System

The Bile

THE liver secretes up to a litre of bile daily and more is formed by day than by night Bile is alkaline and contains electrolytes in the same concentration as plasma the principal organic constituents are—

1 *Bile Pigments* (Fig 14 1) Bilirubin is formed from degenerate red blood cells by the macrophages of the reticulo endothelial system it circulates in the blood stream and is excreted by the liver cells from the vascular capillaries into the bile channels It then undergoes two changes first it is converted into biliverdin in the bile passages by an oxidation process secondly it is reduced in the intestine and excreted in the faeces as urobilinogen (stercobilinogen) which on exposure to air is oxidized into urobilin (stercobilin) Some of the urobilinogen is re absorbed from the intestine into the portal blood and largely re excreted into the bile but there is some spill over into the systemic circulation and this is excreted into the urine as urobilinogen (which on exposure to air becomes urobilin) The bile pigments are excretion products and serve no digestive purpose

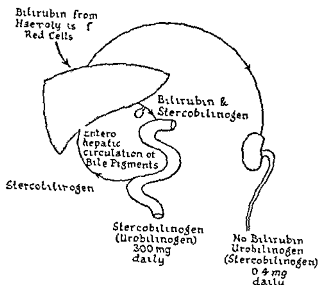


FIG 14 1 NORMAL BILE PIGMENT METABOLISM

2 *Bile Salts* The bile salts are probably formed in the liver They consist of sodium glycocholate and sodium taurocholate and are the main solid constituents of the bile There seems to be a circulation of bile salts they are absorbed completely and do not reach the faeces but instead are carried back to the liver where they are again excreted into the bile It is curious that they do not accumulate in excessive amounts and it is possible that some regulatory mechanisms prevent this Bile salts are essential for the proper emulsification and hence the absorption of fats from the small intestine they are also necessary for the absorption of the fat soluble vitamins from the bowel and assist in the absorption of calcium Their presence in the blood is a powerful stimulus to the production of bile by the liver and in the bile they may help to keep the cholesterol of bile in solution

3 *Cholesterol and Mucin* The cholesterol of the bile may be an excretion from the blood as the concentration in the bile tends to vary with that in the blood Cholesterol is synthesized in the body but when the diet is lipid free the bile cholesterol falls to a lower level

The absence of bile from the bowel as occurs from obstruction in the biliary tree leads to impaired digestion and absorption of fats with corresponding changes in the stools which are typically fatty greasy and of a light putty colour There is a reduced absorption of vitamin K leading to a fall of plasma prothrombin and haemorrhages Retention of bile gives jaundice with pruritus and bradycardia in some cases The blood level of all the organic bile constituents—bile pigments bile salts and cholesterol—are increased bile pigments and bile salts appear in the urine but urobilinogen is absent as it is no longer produced from the bilirubin in the bowel Bile may be lost completely from the body in biliary fistulae there is no longer the injury to the liver that results from prolonged

biliary obstruction and the condition is compatible with health One danger is the loss of water and electrolytes of the bile vigilance is necessary to prevent disturbances from loss of sodium and potassium

The Gall bladder

The gall bladder is a thin walled pear shaped structure 9 cm long with a capacity of about 50 ml of bile The fundus or broad end is directed downwards and forwards and lies behind the right 9th costal cartilage at the outer border of the right rectus abdominis muscle with its junction with the right costal margin It is palpable only when abnormally distended It may be tender when inflamed and sometimes a positive Murphy s sign can be elicited the fingers are hooked up below the liver edge and the patient asked to take a deep breath which causes pain owing to the gall bladder being driven against the fingers The body of the gall bladder extends into the narrow neck which continues into the cystic duct and joins the common hepatic duct to form the common bile duct Hartmann s pouch is a sacculation at the neck where stones tend to lodge The wall of the gall bladder consists of a muscular network without definite layers and including much elastic tissue The mucous membrane which has no glands is in delicate closely woven folds it contains branching invaginations which penetrate into the muscularis (Rokitansky Aschoff sinuses) and plays an important role in acute cholecystitis and gangrene of the gall bladder The function of the gall bladder is to store and concentrate bile the concentration of bile salts pigment, and cholesterol in the gall bladder is 4–10 times that of hepatic bile due to the absorption of water through the gall bladder wall

The sphincter of Oddi is normally contracted and can withstand a pressure of up to 15 cm of water in the common bile duct Therefore the bile which is steadily secreted by the liver is diverted into the systic duct for storage in the gall bladder When the gall bladder is full and if there is no specific stimulus for its evacuation the sphincter of Oddi relaxes and bile trickles into the duodenum During periods of digestion the gall bladder contracts and the sphincter of Oddi relaxes so that the bile is discharged in a gush into the duodenum The most effective stimulus to contraction is the presence of a large amount of fat in the duodenum particularly egg yolk and cream this is probably mediated by a hormone cholecystokinin which is released from the mucosa of the duodenum into the blood stream and carried to the gall bladder and sphincter of Oddi Cholecystokinin is closely related to but not identical with secretin which controls pancreatic secretion Other substances that cause contraction of the gall bladder (cholagogues) are magnesium sulphate pituitrin adrenalin and sympathetic stimulants Atropine is a relaxant The sphincter of Oddi is contracted by morphia and analgesics generally It is little affected by the usual antispasmodics like belladonna or banthine but may be relaxed by the nitrites Normally the gall bladder does not empty itself completely but fills slowly and empties irregularly this is shown by the fact that on a normal mixed diet dye stuffs introduced into the gall bladder are still there up to 3 days or more but not after 7 days Removal of the gall bladder usually gives no ill-effects the bile ducts become dilated to accommodate to some extent the bile which is continually secreted by the liver

Cholecystography A plain film of the abdomen is taken as some gall stones—less than half—contain enough calcium to make them radio opaque The ring shadows faceted if a number are present, are characteristic if necessary a lateral film will distinguish them from renal stones by demonstrating them lying anteriorly in the abdomen The dyes that are used to show up the gall bladder belong to the halogenated phenophthalein derivatives and are given orally the one in current use is telepaque (idiopanoic acid) which is easy to swallow non toxic and produces a highly-contrasting dense shadow Films are taken 12–14 hr later both in the prone and erect position the latter is necessary to show up radio translucent stones which float on the radio opaque layer The patient is then given a fatty meal and a picture taken an hour later to judge post prandial contraction It is little use doing a cholecystogram in a jaundiced patient with the serum bilirubin above 2 mg per cent for the liver will have the same difficulty in secreting the dye as it has in secreting bilirubin Failure of the gall bladder to fill in 12 hr can be due to a number of other causes apart from a diseased gall bladder These are failure of the dye to be absorbed through vomiting or diarrhoea failure of a damaged liver to excrete the dye into the bile ducts a previously unsuspected cholecystectomy an intra hepatic gall bladder concealed by the liver shadow or blockage of the cystic duct by a stone which prevents the dye entering the gall bladder In practice a complete failure of visualization makes gall bladder disease a strong probability if necessary the cholecystogram can be repeated with a double dose of the dye or the intravenous dye biligrafin can be used Biligrafin is particularly useful after cholecystectomy as it enables the cystic hepatic and common bile ducts to be well visualized

The other method of visualizing the biliary tree is by cholangiography This is of value in determining

the patency of the bile ducts and detecting any extra hepatic obstruction It is performed by injecting con trast material usually 50 per cent diodone into the gall bladder during a laparotomy or by peritono scopy or along a biliary drainage tube Its use becoming more common as it increases the ac curacy of diagnosis and prevents many re-explora tions for residual stones

Gall stones

Gall stones have been recognized for centuries yet the mechanism of their formation is still an enigma The nucleus of a stone consists of bile stained organic matter such as epithelial debris or mucus the rest of it is made up of amorphous or crystalline material Some stones consist entirely of cholesterol which is secreted in high concentra tion in the bile and still further concentrated in the gall bladder Cholesterol is held in solution by the bile acids which are powerful solvents of bile due to their surface tension reducing action The ratio between cholesterol and bile salts in the bile is im portant and factors that either increase the amount of cholesterol or alter the bile salt concentration favour precipitation of cholesterol Cholesterol stones are often single and may reach a diameter of 4 cm section shows them to consist of coarse yellow crystals radiating from the centre they are not pig mented by bile and are not seen on plain X ray If infection occurs in a gall bladder containing a cholesterol stone a shell of radio opaque calcium pigment is deposited upon the stone which will then be seen as a ring shadow on the X ray Mixed gall stones are the commonest type and are com posed of cholesterol calcium salts bile pigment and a protein matrix derived from the epithelium of the gall bladder wall These are always multiple and their surface is faceted due to pressure from adjacent structures and they usually contain enough calcium to be radio opaque Pigment gall stones follow the excretion of high concentrations of bile pigments and so are associated with conditions where there is increased breakdown of red blood cells such as acholuric jaundice (spherocytosis) and various types of haemolytic anaemia and these conditions should always be excluded particularly in young people Pigment calculi are black or dark green multiple small amorphous and hard and not often radio opaque

Gall stones are found in about 20 per cent of routine autopsies Females particularly those who are obese and have had many children are afflicted three times more commonly than men This is not surprising for the factors that encourage gall stone formation are those that cause an increased biliary cholesterol concentration these are obesity a high fat diet pregnancy and diabetes The incidence varies in different countries according to the dietetic habits of the people and is higher in certain races it is high in Jewish people and low in coloured races The increased incidence with the increasing number of pregnancies occurs with thin as well as fat women the serum and biliary cholesterol is in creased and there is biliary stasis with delayed gall bladder emptying which increases the opportunity for precipitation of the cholesterol The present theory of the formation of gall stones is that cholesterol crystals result from changes of a physico chemical nature rather than from any in fective precipitation It does not seem that infection is the primary cause of the stones the bile and gall bladder wall are sterile although infection may develop later and increase the tendency to gall stone formation

Gall bladder Disease

Disease of the gall bladder is nearly always associ ated with gall stones and therefore occurs in the middle aged and later age groups being more common in the obese and in women It has to be remembered that gall stones are not infrequently seen in this group and may remain symptomless throughout life The finding of gall stones on X ray may therefore be coincidental and a careful assess men of the association or otherwise between the stones and the symptoms in any particular patient has to be made

Effects of Gall stones Gall stones are symptom less in about 90 per cent of cases and remain in the gall bladder throughout life without the owner being aware of their presence Such silent stones are often discovered incidentally and are not necessarily an indication for cholecystectomy as only a small fraction of such cases develop trouble later Severe and dramatic symptoms arise once the stone leaves the gall bladder acute cholecystitis mucocele or empyema of the gall bladder may result from block age of the cystic duct and colic with jaundice occurs when the stone passes into the common bile duct If it remains in the common bile duct ascend ing cholangitis (Charcot s intermittent fever) can occur or if the stone lodges at the ampulla of Vater acute pancreatitis may arise Gall stones may also penetrate through the wall of the gall bladder or bile duct into other structures such as the duo denum or small intestine and can cause intestinal obstruction by becoming impacted in the ileum where the lumen of the intestine is narrowest Finally carcinoma of the gall bladder usually occurs in association with gall stones but symptoms have usually been present for many years before

malignant change develops and the risk of cancer from silent stones is small

Acute Cholecystitis

The present view is that acute cholecystitis is nearly always due to a chemical inflammation of the gall bladder wall The primary event is obstruction of the cystic duct by a stone the retained bile causes irritation and inflammation of the mucosal lining of the gall bladder At this stage the bile is sterile but infection may take place later There is also a rise in pressure in the gall bladder and it is possible that compression of the blood vessels in the gall bladder wall causes infarction and gangrene in some cases It is likely that occasional cases begin with an acute bacterial process in the gall bladder as this can occur in the course of typhoid and paratyphoid fever without obstruction

Clinical Picture Pain is the presenting symptom and is felt in the epigastrium or right hypochondrium and may be referred below the angle of the right scapula or to the right shoulder from irritation of the diaphragm The severity of the pain may vary from that of an acute abdominal emergency to a less dramatic picture The quality may be a persistent deep seated abdominal ache from distension of the gall bladder with intermittent agonizing paroxysms of biliary colic perhaps started by food or movement There may also be peritoneal pain which is more superficial and localized it is accompanied by tenderness and muscular rigidity on palpation with occasional hyperaesthesia and may be aggravated by deep breathing The patient may be severely prostrated with nausea and vomiting and a raised temperature and pulse rigors may occur

Examination shows tenderness over the gall bladder region If the hand is placed beneath the costal margin the gall bladder is driven against the fingers with a deep breath so that the inspiration *is arrested with a catch —a positive Murphy's sign* The gall bladder cannot usually be felt unless surrounded by a mass of adhesions and inflammation There may be cutaneous hyperaesthesia in the 8th and 9th thoracic segments posteriorly Jaundice is absent unless the stone has reached the common *bile duct* a serum bilirubin is useful for first detecting subclinical jaundice the urine contains excess of urobilinogen The leucocyte count may be somewhat raised with a moderate increase in the percentage of polymorphonuclear leucocytes A plain film of the abdomen will reveal any radio opaque stones

Prognosis The prognosis of acute cholecystitis with conservative treatment is good and the mortality rate probably not above one per cent. This may be due to the use of antibiotics or due to the increasing frequency of surgical removal of the gall bladder which may also account for the fulminating disease being so much less common to day Rarely empyema of the gall bladder or gangrene may develop with a fatal biliary peritonitis Other complications are an ascending cholangitis or cholangio hepatitis sub phrenic abscess or acute peritonitis The usual course is for the acute symptoms to subside within a few days but a recurrence after varying intervals of time is probable

Treatment Acute cholecystitis is treated medically but early co operation between the physician and surgeon is advisable in severely ill patients Surgical intervention is indicated only when there is evidence of spreading infection otherwise elective cholecystectomy is carried out later The patient is confined to bed and given adequate fluids and any food that is fancied Relief of pain is obtained by pethidine and atropine morphia is avoided if possible because it causes spasm of the sphincter of Oddi Sulphonamides are freely excreted into the bile but access to the gall bladder may be prevented by a blocked cystic duct The wide spectrum antibiotics are well concentrated in the bile again in the absence of obstruction and tetracycline is a suitable choice There is little doubt about the value of antibiotics in this disease The secondary bacterial infection involves the wall of the gall bladder and it is here that the effect of an antibiotic is needed it may matter little that obstruction in the cystic duct prevents its concentration in the bile

Chronic Cholecystitis

Chronic cholecystitis is the expected concomitant of gall stones and it is questionable whether the condition ever occurs without the presence of such stones The aetiological factors are therefore identical to those concerned in the formation of gall stones It is probable that physico chemical changes result in the precipitation of cholesterol and other bile constituents so that gall stones develop infection occurs later and further increases the tendency to stone formation The mucosa of the gall bladder becomes ulcerated and scarred and the walls shrunken and fibrotic the contained bile is turbid with a sediment of débris and may contain enough calcium to be seen on plain X rays There may be adhesions from the gall bladder to surrounding structures

Clinical Picture The exact diagnosis of chronic cholecystitis is difficult This is because the *condition* can be quite symptomless and a coincidental finding during the investigation of some other complaint and because there are no specific symptoms or signs

The clinical features are those of abdominal distension or discomfort perhaps coming on after food such as fats and flatulence These are non specific symptoms of several gastro intestinal disorders such as peptic ulcer oesophagitis from hiatus hernia the flatulent dyspepsia with aerophagy that is unaccompanied by any organic changes nervous dyspepsia and chronic pancreatitis Chronic cholecystitis is therefore frequently an exclusion diagnosis and should not be made without the necessary investigations to exclude other disorders Physical examination is usually negative Tenderness over the gall bladder may be an unreliable sign particularly in the presence of obesity and can be mistaken for a tender duodenum The question of whether the gall bladder functions well as judged by cholecystography in spite of the gall stones is not of great help perhaps the symptoms are more likely to be due to gall bladder disease with a non functioning gall bladder but this is not necessarily so

Treatment When the diagnosis of chronic cholecystitis is made the correct treatment is cholecystectomy an operation with a mortality of 1 per cent or less This involves exploration of the common bile duct with perhaps operative cholangiography to avoid leaving behind any calculi Medical treatment may be necessary in those cases unfit for surgery This may alleviate symptoms but there is no evidence that the course of the disease is in any way altered otherwise There is no indication for dietetic restriction except for a reducing diet in obese patients and when pain occurs after eating certain foods It is then best to be guided by the patient who will eliminate any foods that cause pain Most patients with gall bladder disease can enjoy and digest fats perfectly well fat intolerance frequently develops only after medical advice to avoid eating fats Fat in the duodenum stimulates the contraction of the gall bladder and the flow of bile, so that it would seem more rational to allow fat to avoid stasis in the gall bladder Medical measures in the treatment of chronic cholecystitis are often unsatisfactory pain relieving drugs and antibiotics may be needed during any acute episodes

Post-cholecystectomy Symptoms Symptoms are not uncommon after removal of the gall bladder particularly if no stones are found The most likely cause is wrong diagnosis and a search must be made for some other explanation of the symptoms Residual stones may be present in the bile duct and these can be missed even after thorough exploration at the time of cholecystectomy it is possible that they may migrate from the hepatic ducts and fresh ones can probably form in the bile ducts after removal of the gall bladder A traumatic bile duct stricture may give similar symptoms to a residual stone and fortunately the new dye biligrafin can be used intravenously to outline the biliary passages after cholecystectomy If no cause is found for the symptoms the condition of biliary dyskinesia can be evoked This is thought to be due to a disturbance of motility Spasm of the sphincter of Oddi is postulated so that there is a rise in pressure in the biliary tract which stimulates biliary colic similar to an impacted stone It is said to occur with or without the presence of a gall bladder Treatment is by anti spasmodics such as amyl nitrite or probanthine or even division of the muscle of the sphincter of Oddi The condition is not open to exact diagnosis and its existence is doubted by some authorities

Malignant Disease of the Gall bladder and Bile Ducts

Carcinoma of the gall bladder usually develops in association with gall stones and chronic inflammation and there is a long history of symptoms due to gall bladder disease The recognition of malignant change is not easy and often the first sign is a hard palpable mass in the region of the gall bladder or general signs of malignant disease such as loss of weight Carcinoma arising in the rest of the biliary system causes obstructive symptoms similar to gall stones and is often only recognized at laparotomy

Diseases of the Liver

The liver the largest organ in the body is the centre of metabolism. It synthesises the plasma proteins prothrombin fibrinogen and heparin it stores glycogen and regulates the blood sugar and is vital in fat as well as carbohydrate metabolism It is a storage organ for substances such as vitamins glycogen and fats It is an excretory organ mainly for bile and protects the body by detoxicating unwanted or injurious products not only the by products of metabolism but also drugs a practical example of this is morphine which in customary doses can be dangerous in the patient with liver disease Finally it contains the main part of the reticulo endothelial system and therefore is involved in the various diseases of this system such as the reticuloses and lipoid storage diseases

Total removal of the liver in animals results after a few hours in a fatal hypoglycaemia unless relieved by giving sugar the blood urea falls with a concomitant rise in amino acids as the liver is the

chief site of deamination of amino acids and the only organ where urea is formed coagulability of the blood is depressed from decrease in plasma prothrombin jaundice develops regularly in animals surviving longer than six hours various non specific symptoms of hepatic insufficiency occur if the blood sugar is kept normal—restless ness dyspnoea vomiting ataxia anuria and coma —from loss of some unknown liver functions

The clinical aspects in man are modified by the remarkable physiological reserve and great re generative power of the liver as shown by the strik ing nodules of new liver tissue seen in cirrhosis Chronic severe liver disease may therefore occur without symptoms Liver cell failure is most evident by jaundice apart from this there are numerous rather non specific symptoms of ill health and nervous system involvement from among which the typical tremor the liver flap has recently been separated Portal hypertension due to fibrosis strangulating the branches of the portal veins gives a characteristic sequence of events with ascites and the formation of anastomotic vessels such as oesophageal varicose veins that may rupture and result in fatal haemorrhage

The lower edge of the liver can frequently be felt in normal subjects particularly if they take a deep breath or are emphysematous A palpable liver is not necessarily an enlarged one Percussion deter mines both the upper and lower edge though it is inaccurate in obese subjects The detection of a definitely hard liver may be more reliable evidence of disease than the complex liver function tests but the surface consistency is an unreliable physical sign as nodularity may be confused by feeling fat deposits in the subcutaneous tissues

INVESTIGATION OF LIVER FUNCTION AND PATHOLOGY

Bilirubin which causes jaundice is derived mainly from the haemoglobin of destroyed red blood cells It is a waste product excreted by the liver through the biliary system into the intestine the other breakdown products of haemoglobin are retained in the body for further use in blood formation the iron being stored in the reticulo endothelial cells and the globin used again for the protein molecule The bilirubin after concentration in the gall blad der is injected into the intestine where by bacterial action it loses its green colour and changes into the brown pigment stercobilinogen

Some stercobilinogen is absorbed from the gut into the portal circulation and re excreted by the liver into the bile A minute amount spills over from the liver into the systemic circulation and is excreted in the urine where it is named urobilino gen a colourless compound which oxidizes when the urine is left standing and is converted into the yellow pigment urobilin Urobilinogen is excreted in minute amounts less than 0 4 mg daily in nor mals and does not give positive qualitative tests This absorption of bile pigments from the gut and their re-excretion by the liver is called the entero hepatic circulation of bile pigments It does not seem to benefit the organism but is useful in diag nosis Urobilinogen disappears from the urine in obstructive jaundice as no bilirubin appears in the intestine but is increased when bilirubin production is increased as in haemolytic anaemia or when the failing liver cell cannot re excrete the normal amount absorbed from the gut

Causes of Jaundice

1 *Increased Production of Bilirubin* (Haemo lytic Jaundice Fig 14 2) Increased breakdown of red blood cells results in increased production of bilirubin The red cells themselves may be defective with greater fragility as in congenital haemolytic jaundice or have a shorter life as in pernicious anaemia Haemolytic anaemia may result from cir culating haemolysins or occur after incompatible

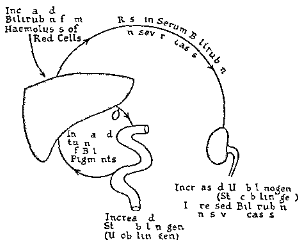


FIG 14 2 HAEMOLYTIC JAUNDICE

blood transfusion and in the physiological jaundice of the new born or from Rhesus blood factors Malaria and blackwater fever are other examples of haemolytic anaemia

Clinically the jaundice is usually slight and the lemon tinge contrasts with the deep greenish colour of obstructive jaundice Pruritus and bradycardia do not occur The liver speeds up the excretion of the bilirubin and so the stools are darker from

greater amounts of stercobilinogen Increased quantities of stercobilinogen are absorbed from the gut and appear in the urine giving positive tests The freshly voided urine is of normal colour as no bilirubin is present but darkens on standing because of the oxidation of the excess urobilinogen

2 *Liver Failure* In liver failure the liver cell is unable to excrete the normal amounts of bilirubin which is retained in the blood Frequently there is swelling of the cells and oedema which blocks the bile canaliculi and causes regurgitation of bilirubin into the blood stream adding an intrahepatic obstructive element (*see* Fig 14 3) This type of jaundice is seen in virus hepatitis portal cirrhosis and from liver poisons such as phosphorus chloroform arsphenamine carbon tetrachloride cinchophen and trinitrotoluene

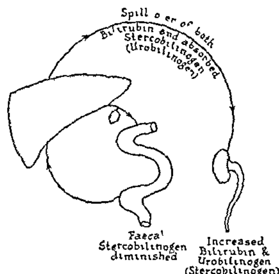


Fig 14 3 Jaundice in Hepatitis

The serum bilirubin is raised and there may be excess urobilinogen in the urine in pure liver-cell failure as the liver cannot deal with the absorbed stercobilinogen When the intrahepatic obstructive element is marked the stools become pale from absence of stercobilin and urobilinogen disappears from the urine The reappearance of urobilinogen in the urine in infective hepatitis is therefore a good prognostic sign indicating a diminution of the oedema and swelling of the liver cells

3 *Obstructive Jaundice* (Fig 14 4) This occurs from lesions anywhere in the biliary system that block the flow of bile from the liver to the duodenum Common causes are gall stones which usually make their presence obvious by colic in contrast to the painless onset of jaundice in the elderly which results from carcinoma of the head of the pancreas Other causes include carcinoma of the ampulla of Vater or of the gall bladder or bile ducts or involvement of the glands of the porta hepatis and cholangitis usually associated with cholecystitis or strictures following gall bladder surgery Drugs such as chlorpromazine (Largactil) and methyl testosterone also can cause an obstructive type of jaundice

Clinically the jaundice is usually marked the stools are light from excess fat and absence of stercobilinogen and the urine dark from bilirubin.

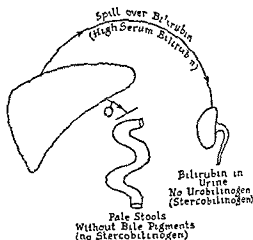


Fig 14 4 Obstructive Jaundice

Urobilinogen disappears from the urine when the obstruction is complete as no enterohepatic circulation of bile pigments takes place A greenish tinge in the skin appears when the jaundice is deep and prolonged probably from conversion of the bilirubin to other pigments such as biliverdin there is bradycardia which may be due to increased vagal tone from circulating bile salts There is a tendency to haemorrhage from defective absorption of vitamin K from the absence of bile salts with consequent increase in the coagulation time of the blood due to prothrombin deficiency When the obstruction is complete the jaundice is progressive with little fluctuation in its depth yet the serum bilirubin levels may vary probably from alterations either in bilirubin production or in renal excretion

Differential Diagnosis

Chemical Tests

Measurements of bile pigments in the serum and urine are valuable in the differential diagnosis of jaundice Routine measurement of the stercobilinogen in the stools is not practicable but the daily recording of the colour of the faeces is a valuable and essential clinical investigation

Tests on the Serum (Serum Bilirubin) This is a colorometric method using Ehrlich s diazo reagent which is added to the serum with alcohol The normal level is 0 4 to 1 0 mg/100 ml In haemolytic anaemia the levels are usually about 1 5 mg/100 ml but may rise to 5 mg or higher during crises In complete obstruction from carcinoma of the pancreas there is a progressive rise in serial readings whereas these like the colour of the stools may fluctuate with a gall stone impacted in the bile duct

The van den Bergh reaction is dependent also on the use of Ehrlich s diazo reagent but divides the bilirubin in the serum into the direct and indirect types The amount of colour developing in the first minute after adding the reagent is thought to represent bilirubin that has regurgitated from the biliary tree because of obstruction whereas the colour developing after ten minutes indicates bilirubin thought to be attached to protein which has not passed through the liver cells These assumptions are not supported by electrophoretic studies as it seems that all bilirubin in the serum is attached to protein and the exact explanation is not yet known The test is of limited practical value and is useless if the serum bilirubin is above 3mg/100 ml as a direct result then occurs in all types of jaundice It may be helpful in slight jaundice when an indirect result is usually associated with haemolytic jaundice

Tests on the Urine Bilirubin is excreted in the urine in both obstructive and parenchymatous jaundice but is not found in the urine in haemolytic jaundice unless the jaundice is unusually deep

The urine is yellow orange and a simple test for bilirubin is to shake the urine when the froth will be coloured yellow

The most satisfactory test for bilirubin in the urine is the Tablet test This also makes use of a diazo dye and is based on the same principle as the van den Bergh test for serum The method is very sensitive and specific for bilirubin

Fouchet s reagent is used in the Harrison spot test and this is also accurate

The iodine and nitric acid ring tests which depend upon the oxidation of bilirubin to green biliverdin are not now considered sensitive enough to justify their routine use

Urobilinogen is found in the urine when there is excessive pigment formation from haemolytic anaemia or when the liver cells cannot excrete the absorbed stercobilinogen from the intestine It is absent in obstructive jaundice Ehrlich s reagent is used and a quantitative daily measurement can be made when necessary Fresh urine must be used and an afternoon specimen when the excretion is at its maximum is representative of the 24 hr period Schlesinger s method is used when the urine is not fresh and is probably the best routine test

Tests of Liver Function

Protein Metabolism These tests detect alterations in the serum proteins the synthesis of which depends upon the healthy liver cell Estimation of the serum albumin is necessary as it is decreased below 4 g per cent in long standing liver disorder such as hepatitis or cirrhosis and the serum globulin is frequently raised above 2 8 g per cent The various flocculation tests of the serum detect an imbalance of the various protein fractions rather than any quantitative differences and attempts have been made to correlate them with the electrophoretic pattern of the serum It seems that the colloidal gold precipitation and zinc sulphate turbidity reflect changes in the γ globulin being positive in portal cirrhosis whereas the thymol turbidity and flocculation tests assess the lipo protein or β globulin changes and indicate inflammatory changes such as in infective hepatitis rather than cellular damage

These tests may be positive in other diseases where there is hyperglobulinaemia especially with involvement of the reticulo endothelial system These include infectious mononucleosis leukaemia malaria myelomatosis and collagen diseases including rheumatoid arthritis

Other tests of liver functions are numerous The serum alkaline phosphatase levels may be raised and parallel the obstructive factor in the jaundice whether this is intra or extrahepatic This test is also positive in certain bone lesions The origin of the enzyme is unknown and the reason for the retention in the blood stream in biliary tract obstruction and to a lesser extent in liver cell damage is also not clear The total serum cholesterol is raised in chronic obstruction of the bile ducts but low values are found in portal cirrhosis with liver failure and indicate a bad prognosis particularly if the cholesterol ester is depressed or absent Similarly a failing liver cannot maintain

the prothrombin content of the blood and this if abnormal is unaffected by giving vitamin K in contrast to the low prothrombin levels found in other conditions The bromsulphalein tolerance test is useful in detecting liver damage in the absence of jaundice such as in cirrhosis The serum bilirubin must be less than 2 mg per cent and the dye is injected intravenously It is removed from the serum by the liver within 45 minutes in normals but is retained when the liver damage is present

Severe liver disease such as cirrhosis or malignant deposits may be present although all the liver function tests may be negative Usually the diagnosis can be made on clinical grounds but a final court of appeal in obscure diffuse liver disease is aspiration needle biopsy This is an investigation that can be carried out under local anaesthesia at the bedside It is preferably done in hospital because of the slight risk of bleeding though, in skilled hands the mortality rate is a great deal less than that of laparotomy As a research procedure it has contributed much knowledge about the pathology of infective hepatitis and it is occasionally essential in clinical practice But most cases of jaundice can be diagnosed by a careful history and appropriate investigations and where an anastomosis may have to be performed it is better to advise a laparotomy

VIRUS INFECTIONS OF THE LIVER

The liver is susceptible to certain viruses which cause diffuse liver cell damage Fortunately it is unusual for this to be fatal a fact that explains why the pathology has been elucidated so recently Much knowledge has been obtained from liver function tests and in particular serial liver biopsy studies It is now clear that an acute virus hepatitis is the true explanation of so called catarrhal jaundice, epidemic jaundice homologous serum hepatitis post transfusion and post vaccinal hepatitis as well as post inoculation or syringe hepatitis It explains the jaundice occurring in venereal disease clinics A virus infection probably accounts for the acute yellow atrophy of the older writers and it may result in a pathological picture indistinguishable from portal cirrhosis

Infective Hepatitis

This is associated with the virus IH and is present in faeces in great concentration It has been shown by human transmission experiments to be conveyed by faecal contamination and is therefore a disease of bad hygiene This explains its prevalence in war time when its appearance in epidemic form in armies may create difficult military problems There is as yet no evidence of other modes of spread such as by nasopharyngeal droplets

There is an acute inflammation of the entire liver Necrosis and autolysis of the liver cells is particularly marked in the centres of the lobules and this centrilobular necrosis is characteristic of a virus infection leucocytic infiltration is present and there may be extreme disorganization of the hepatic cells yet the reticulum framework is strikingly well preserved and may provide a scaffolding upon which the globule is reconstructed an event that occurs in most cases Occasionally the severity of the infection creates such devastation that restoration of the liver lobule is no longer possible and liver cells regenerate in a nodular fashion Cirrhosis with proliferation of connective tissue usually follows This post hepatitis cirrhosis may rarely be complicated by primary liver-cell carcinoma An associated inflammation of the alimentary tract may occur and casts may be found in the urine A mild meningo-encephalitis or haemorrhages into the brain may give neurological symptoms, haemorrhages usually from prothrombin deficiency may be found in the lungs intestines kidneys and elsewhere in fatal cases

Clinical Picture The incubation period varies from two to six weeks Most cases start suddenly in young people with a typical pyrexial illness Often there is a pre icteric stage so that the illness presents as pyrexia of unknown origin The astute may foretell the onset of jaundice by the following features—

A striking nausea and distaste for food

Nausea and vomiting with tenderness of the liver

Bilirubin in the urine which in the majority of patients appears before jaundice

Excess urinary urobilinogen in some patients because the damaged liver cell cannot re excrete into the bile all the urobilinogen absorbed from the intestine

When the jaundice appears the patient usually begins to feel better The temperature disappears the appetite returns and the upper abdominal symptoms such as distension and vomiting subside The jaundice which is partly due to cellular damage and partly to intra hepatic obstruction from engorgement of liver cells results in dark bile stained urine and clay coloured stools the latter

may cause transient diarrhoea from their fatty content Concomitants of jaundice such as bradycardia and pruritus occasionally occur Most patients have a tender hepatic enlargement though usually slight

Diagnosis This in the presence of jaundice is usually obvious Certain of the liver function tests such as the zinc sulphate and thymol turbidity flocculation may be positive due to a qualitative but not quantitative change in the serum proteins These are particularly important in the unusual case which presents as obstructive jaundice so that unnecessary laparotomy can be avoided Liver biopsy is rarely indicated as a diagnostic measure

Course The clinical picture has wide variations Many cases are undiagnosed as they do not have jaundice and the illness is mild On the other hand fulminating cases who die from acute liver failure or later from cirrhosis of the liver are seen The overall mortality is however very low and the illness after the initial stage is mainly an inconvenience only to most of the sufferers and lasts about six weeks Signs of recovery are the disappearance of bilirubin from the urine and the appearance of this pigment in the stools Inflammatory changes may persist in the liver long after recovery of the patient These may give rise to the post hepatitis syndrome consisting of malaise easy fatigue and a feeling of being run down such non specific symptoms however can easily be induced by the over cautious approach of the medical attendant

Treatment It is unlikely that any treatment alters the natural course of this disease Bed rest is unavoidable in the early stages and is usually continued until the jaundice is obviously disappearing more prolonged rest does not in controlled series result in lessening of any sequelae The patient is allowed to eat what he fancies as there is no indication for the traditional low fat high carbohydrate diet controlled dietetic studies even suggest that a high fat diet gives better results and a high protein diet not only fails to improve the prognosis but may be harmful when there is danger of liver coma in severely ill patients In hospital the patient is barrier nursed with the infected stools being disposed of as in typhoid fever Human serum γ-globulin gives protection to contacts and can be considered in the rare instances where this is desirable

Serum Hepatitis

This disease similar to infective hepatitis in its clinical and pathological aspects is probably identified with a different virus SH Its incubation period is longer from six weeks to six months It is unprotected by γ globulin and the virus has no cross immunity with the virus of infective hepatitis The latter is commoner in younger people as the elderly develop immunity this does not occur in serum hepatitis which appears in all age groups

The importance of serum hepatitis is that it is an iatrogenic disease which like infective hepatitis is occasionally fatal It is transmitted by any procedure where a needle or other instrument is used on more than one patient and whenever blood or its products are injected The former include subcutaneous intramuscular intravenous and all other forms of puncture and is due to contaminated serum remaining in the needles syringes or other equipment used The latter is more likely from plasma infusion therapy because the pooling of the plasma increases the chance of one of the donors being a carrier of the virus Epidemics have occurred in diabetic and venereal disease clinics

It is prevented by proper sterilization of instruments No chemical disinfectants are satisfactory Heat must be used and this is more effective if all equipment is washed thoroughly after use in order to rid it of organic material such as blood coagulating on its surfaces The following methods of applying heat are available—

1 Boiling in water It is however thought possible that the virus may even survive 10 minutes boiling The following methods of sterilization should therefore be used whenever possible
2 Autoclave (steam under pressure)
3 Dry heat sterilization (hot air oven) Usually 170 C for 30 minutes
4 An open flame can be used for lancets used in capillary blood sampling and for scarification used for vaccination

Blood donors are potential vectors of the disease but there is as yet no practical means of detecting carriers of the virus Nor is there any method of destroying the virus in blood or plasma and it survives both being dried and frozen

Infectious Mononucleosis (Glandular Fever)

The classical case of infectious mononucleosis (*see* p 504) is easy to recognize but the clinical variations are such that it may mimic other diseases Beginning as a pyrexia of unknown origin and causing as occasionally happens a hepatitis the similarity to infective hepatitis may be great Distinction lies in the enlargement of glands the blood picture with glandular fever cells and a positive Paul Bunnell test where the heterophile antibodies are in contrast to the occasional positive result in infective hepatitis not absorbed by guinea pig

kidney Needle liver biopsy studies have also shown a different pathology There is an infiltration of the liver with large mononuclear cells similar to those in the peripheral blood The typical centrilobular necrosis of infective hepatitis is not seen although there may be focal necroses

Yellow Fever

This is an acute virus infection transmitted to man by the bite of a mosquito The virus particularly involves the liver kidneys and heart It may give extensive liver necrosis but the architecture remains intact and cirrhosis does not follow it

SPIROCHAETAL INFECTIONS

Weil's Disease

Weil s disease or spirochaetal jaundice begins in a similar way to infective hepatitis with which it can easily be confused The organism *Leptospira icterohaemorrhagica* is present in the tubules of rat s kidneys and from this reservoir the leptospira are constantly excreted in the urine they then live for months in pools damp soil or canals The portal of entry into man is probably through abrasions in the skin and perhaps the alimentary or respiratory tract The disease therefore is mostly seen in agricultural or sewer workers coal miners and fish cutters in the last it is recognized as an occupational disease for which compensation is allowed

The pathology of the liver is that of a mild hepatitis It differs from infective hepatitis in the absence of centrilobular necrosis and of sequelae such as cirrhosis The reason for the jaundice is not straightforward as patients with deep jaundice may show only slight histological changes in the liver It is possible that production of bilirubin is increased by absorption of haemorrhages retention in the serum results from the damaged liver and the accompanying tubular necrosis in the kidneys prevents excretion in the urine

Clinical Picture The disease begins with septicaemia when the leptospira are present in the peripheral blood There is high fever and prostration The temperature gradually subsides in about a week Other features are abdominal symptoms especially pain and vomiting which may suggest an abdominal emergency conjunctivitis central nervous system symptoms usually due to a meningeal infection and symptoms of an upper respiratory tract infection A minority of the patients develop haemorrhages probably from a direct toxic action of the leptospira on the capillary wall and these may occur in the skin gut lung or elsewhere During the second or toxic stage the temperature falls but the patient does not improve jaundice deepens blood pressure falls the heart dilates and death may follow from uraemia The leptospira are found in the urine and the serum shows a rising antibody titre

There are many variations of this clinical picture Some patients do not develop jaundice and the outlook is good In the presence of jaundice the mortality is between 10 and 20 per cent. Permanent hepatic or renal changes do not occur

Diagnosis In the first stage it may mimic septicaemic illness When jaundice appears it is distinguished from infective hepatitis by the following—

1 The conjunctival injection
2 Muscle pains
3 Severity of prostration
4 Albuminuria
5 A polymorph leucocytosis
6 A positive leptospiral agglutination test, particularly with a rising titre
7 Leptospira in the blood stream in the first week and in the urine afterwards

Treatment Prevention is by protective clothing to the lower extremities where abrasions may present portals of entry for the organism and the extermination of rats Specific immunization serum is valuable to exposed workers and during the first week of illness but it is rarely diagnosed before the jaundice occurs Penicillin in large doses 10 to 20 mega units daily is given for three or four days and is usually effective if not another antibiotic such as tetracycline is tried Complications such as anuria will need the specialized therapy for this condition

Other Rare Spirochaetal Infections of the Liver

There are numerous species of leptospira pathogenic to man and canicola fever due to *L canicola* a common infection of dogs can be transmitted to man It is clinically indistinguishable from Weil s disease but is more benign and fatalities are unknown Diagnosis is similar to Weil s disease and the rising antibody titre is specific It usually however presents as a benign aseptic meningitis

The jaundice of syphilis is usually infective hepatitis and the use of adequately sterilized syringes and needles has greatly reduced the incidence It is possible for the jaundice to result from arsenical or penicillin treatment as a Herxheimer reaction

occurring about nine days after beginning treat ment or as an allergic reaction to arsenic giving an intrahepatic obstructive type of jaundice Con genital syphilis may involve the liver as the foetal circulation results in this organ being heavily in fected from transplacental blood There is a diffuse hepatitis giving a true cirrhosis which is called a pericellular cirrhosis owing to the distribution of the fibrous tissue Jaundice may occur from secon dary syphilis The typical lesion of tertiary syphilis is the gumma which heals with deep scarring giving the hepar lobatum and cirrhosis does not occur

PROTOZOAL INFECTIONS

These may occasionally be seen in Britain and per haps may increase as transport from tropical zones becomes more easy and frequent

Schistosomiasis (Bilharziasis) due to *Schistosoma mansoni* is prevalent in Africa Egypt South America and the West Indies Eggs are excreted in the faeces of patients and hatch out in water giving free swimming embryos These enter certain species of snails and develop into fork tailed cercariae which re enter human skin in contact with infected water There is blood stream dissemination and they finally lodge in the intrahepatic portal system and grow rapidly Both liver and spleen are en larged Eventually fibrosis and portal hypertension result Aspiration liver biopsy is diagnostic Pre vention is by sterilization of infested water Treat ment with antimony is of value in early cases only

Entamoeba histolytica has a world wide distri bution and causes amoebic hepatitis or amoebic abscess of the liver in the tropics In the former there are focal necrotic areas throughout the liver which result in scars A large liver abscess is pro duced by the cytolytic enzyme of the amoeba The so-called pus is really necrotic liver tissue and frag ments of liver can be recognized in it it resembles anchovy or chocolate sauce Both of these are acute conditions and the existence of chronic amoebic hepatitis is like the post hepatitis syndrome a somewhat doubtful entity Diagnosis and treatment of amoebiasis is discussed on p 109 Liver involve ment is indicated by pain in the liver area with hepatic enlargement particularly of the upper edge and occasionally jaundice Liver function tests often do not help but a plain X ray of the upper abdomen may show an enlarged liver shadow with an elevated right diaphragm Aspiration of a liver abscess may be necessary for diagnosis and treat ment Cirrhosis of the liver does not occur after amoebic infection

Other Infections Septic conditions of the liver are rarely seen now owing to the rarity of chronic purulent conditions in the peritoneum such as appendix abscess and their early treatment by anti biotics The liver has a curious immunity against tuberculosis

VASCULAR CATASTROPHES AFFECTING THE LIVER

Hepatic Artery Occlusion

This rare event may follow surgical trauma particularly during gall bladder operations Medi cal causes are emboli from bacterial endocarditis or direct invasion from malignant glands in the porta hepatis There is a sudden pain in the right hypochondrium with collapse fall in blood pres sure and slight jaundice with infarction of an area of the liver Other features of an infarction follow—pyrexia leucocytosis and a raised sedimen tation rate There is a sudden increase in the pro *thrombin time with haemorrhagic manifestations* It is usually fatal

Hepatic Vein Occlusion (Budd Chiari Syndrome)

Aetiological factors are direct invasion of the veins from adjacent neoplasms thrombo phlebitis or other conditions associated with thrombotic ten dencies such as polycythaemia The liver shows changes similar to congestive cardiac failure

The clinical picture is that of an ill patient who develops sudden pain in the right hypochondrium with slight but not severe jaundice There is sud den vomiting and liver enlargement with ascites

The condition should be considered when a patient usually ill already develops an enlarged liver with gross ascites resistant to treatment

Acute occlusion of the entire hepatic vein results in death from liver failure A chronic type of venous occlusion causes episodes of vague indiges tion hepatomegaly and ascites This is followed by all the features of portal hypertension

Portal Vein Thrombosis

Acute thrombosis is rare and may follow splenec tomy particularly in patients with a normal platelet count

Thrombosis is a common sequel of portal cir rhosis due to the slowness of the portal blood flow and may be seen in polycythaemia vera or as a

result of direct invasion of the vein from malignant disease

If the liver is normal there is no jaundice nor any evidence of liver disease as shown by liver function tests or biopsy, and cirrhosis does not follow In the usual case with cirrhosis and low serum proteins ascites follows The picture is frequently that of a patient with a well compensated cirrhosis who develops a transient ascites or episodes of mental change

OTHER DISEASES OF THE LIVER

Cirrhosis

Cirrhosis is the common end result of liver damage from various agents and the cause cannot be recognized from the histology The word of Greek origin means tawny and was first used by Laennec to describe the slightly jaundiced colour of the projecting nodules Cirrhosis is not synonymous with fibrosis and is used when connective tissue proliferation with disturbed hepatic architecture occurs with nodular regeneration and hepatic cell necrosis Half the cases in Britain are of unknown origin Some particularly those with a past history of jaundice may have resulted from infective hepatitis but the true incidence of this as a cause will be discovered only when there are effective tests for various virus infections Alcohol as a cause varies from country to country and alcoholic cirrhosis is not commonly seen in Britain Cirrhosis may occur in certain long standing alimentary disorders such as ulcerative colitis and may be seen in the congested liver of heart failure if the patient lives long enough It is a characteristic feature of some interesting but obscure disease such as haemochromatosis and hepatolenticular degeneration and may follow parasitic infestations like bilharzia Biliary cirrhosis follows biliary obstruction Nutritional lack plays no part in cirrhosis in temperate zones and there is no proved connexion between fatty liver and cirrhosis

Clinical Picture Some cases are discovered coincidentally during life or at autopsy by the finding of an enlarged liver and spleen and are symptomless and may not shorten life

Symptoms occur most frequently from circulatory disturbances due to fibrous strangulation of the portal venous system with subsequent portal hypertension This gives ascites and haemorrhage from the upper gastro intestinal tract due to anastomotic varicose veins in the lower oesophagus and fundus of the stomach The rest of the clinical picture which may terminate in hepatic coma is due either to liver cell failure or to diversion of the products of digestion and toxic sub tances directly into the systemic circulation through anastomotic channels rather than into the liver where they are usually metabolized or detoxified

There is frequently a deterioration of general health with weakness weight loss anorexia and vague indigestion A low grade fever may be seen this may result from the products of necrosing liver tissue or from coliform ba t ria passing directly into the blood stream without the liver acting as a possible filter Foetor hepaticus gives the breath a characteristic smell sweetish and fishy A macrocytic anaemia usually not severe may be present and it fails to respond to vitamin B_{12} or folic acid

Neurological changes may herald hepatic coma Mental symptoms such as confusion amnesia and hallucinations may be intermittent at first but later pass into stupor A flapping tremor of the outstretched arms or of other parts of the body giving the trombone movement of the tongue is almost specific for liver failure and there may in addition be a fine tremor of the fingers slightly faster than in Parkinsonism Both types of tremor disappear at rest There is no single explanation for hepatic coma which is hardly surprising as the liver has so many functions One important aspect from the practical side is that nitrogenous substances in the intestine may precipitate coma due probably to the resulting high blood ammonium levels A high protein diet drugs su h as ammonium chloride or urea and blood in the intestine from ruptured varices may be dangerous

Jaundice is serious as it often heralds liver failure Complications of portal cirrhosis are portal vein thrombosis and rarely hepatoma from carcinomatous change

Chronic pancreatitis sometimes occurs with cirrhosis The reason for this is unknown but it is possibly due to protein deficiency Another associated disease is glomerulo nephritis Pulmonary tuberculosis used to be a common cause of d ath among cirrhotics but is now quite rare

Diagnosis The liver is enlarged and hard in the early stages of cirrhosis but is usually shrunken and small when portal hypertension and ascites have occurred Splenomegaly is expected If the abdominal wall is thin the irregular surface of the liver can be detected The skin particularly in the upp r half of the body should be searched for the diagnostic spider angiomas These are probably of endocrine origin and there may be changes such

as atrophy of the testes and prostate or gynaecomastia in men and atrophic breast changes in women before the menopause These are thought to result from inability of the liver to inactivate hormones Reddening of the palms of the hands liver palms may be seen but occur in other diseases such as rheumatoid arthritis

Diagnosis is confirmed when oesophageal varicose veins are demonstrated Liver function tests may be negative in the quiescent symptomless phase but the bromsulphalein retention tests usually show impairment A final court of appeal is aspiration liver biopsy but clinical diagnosis is usually possible without it

Treatment No treatment is indicated for the symptomless cirrhotic A normal diet is allowed but alcohol being a liver poison should be avoided

Ascites may have to be relieved by paracentesis but is best controlled by a rigidly low salt diet together with mercurial diuretics or chlorothiazide

Bleeding from oesophageal varices is a serious symptom and often fatal Death may occur from haemorrhage alone or from liver cell failure caused by hypotension analagous to renal failure in extra renal uraemia and hepatic coma may be precipitated due to nitrogen from blood absorbed in the gut The blood volume must be maintained by drip transfusion especially with packed cells Oesophageal compression tubes such as that devised by Sengstaken have reduced the mortality The three lumen tube is passed into the stomach through the mouth The gastric balloon is inflated and some traction applied by fixing it to the nose by adhesive tape this blocks the veins of the fundus of the stomach through which blood enters the oesophageal varices A further sausage shaped balloon can be inflated in the lower oesophagus giving direct pressure to the veins Nurses must be warned of the danger of the balloons entering the pharynx where they may cause suffocation if there is any such sign the tube should be cut with scissors and withdrawn Apart from emergency treatment of bleeding oesophageal veins there are operative procedures to anastomose a vein of the high pressure portal system to the low pressure caval system the splenic vein may be joined to the renal vein or the portal vein directly to the inferior vena cava Other methods are to inject the veins with sclerosing solutions or resect or ligate them There has so far been no adequate follow up of this surgery but results are not encouraging and the prognosis really depends upon the functional capacity of the liver cells

The routine management of the patient with chronic liver failure consists of symptomatic measures Patients should eat well with a high calorie diet both of protein and carbohydrate as glycogen laden cells are more resistant to toxic injury The protein may however have to be lowered at the first sign of neurological complications usually a daily amount of 50 g is then satisfactory but protein may have to be eliminated altogether if coma is impending Other nitrogen containing compounds such as ammonium chloride and urea must be avoided Sedatives provide a difficult problem as most are detoxicated by the liver and have a prolonged action in patients with liver failure Morphia barbiturates and paraldehyde should all be given first in small doses

No specific measures are available for the treatment of hepatic coma Fluid and electrolyte balance must be maintained and a wide range antibiotic should be used to inhibit the bacteria in the gut from breaking down the nitrogen containing substances

Biliary Cirrhosis

This rare form of cirrhosis follows chronic biliary obstruction The surface of the liver shows a fine irregularity without the nodular regeneration of portal cirrhosis It is dark green from bile staining and the distention of the bile system It is never small It may follow any type of biliary obstruction and is more likely when an intermittent or partial obstruction is associated with ascending biliary infection Rarely a primary biliary obstruction occurs where the lesion may be in the small bile radicles

Every case should be submitted to laparotomy with exploration of the bile ducts or an operative cholangiogram to detect any treatable cause for the obstruction Without this the condition is always fatal Symptomatic treatment consists of methyltestosterone 25 mg sublingually or corticotrophin to relieve pruritus Fat soluble vitamins A D and K have to be injected at about monthly intervals as they are not absorbed from the intestine and additional calcium should be taken daily to prevent osteomalacia Antibiotics may be needed when there is ascending cholangitis

Hepatolenticular Degeneration (Wilson s Disease)

This is an inborn error of metabolism which is inherited recessively and affects young age groups It is due to a disturbance of copper metabolism where a deficiency of copper binding plasma protein results in increased absorption of copper from the alimentary tract This copper instead of being firmly bound in the serum is deposited in the liver and brain It is also excreted in the urine and later deposited in the kidney and renal tubules causing an amino aciduria

The patients usually present with neurological

symptoms such as tremor or rigidity from basal ganglia involvement and this may mimic Parkin sonism (*see* p 448) The liver and spleen may be palpable from cirrhosis of the liver and the finding of a Kayser Fleischer Ring a pigmented golden ring at the periphery of the cornea may be seen with the naked eye or with the slit lamp

B A L is used but follow up results are not yet available Chelating agents which are substances used in industry to inhibit reactions normally cata lysed by trace elements are also used to remove copper from the body

Haemochromatosis (Bronzed Diabetes) (*see* p 164)

This is an inborn error of metabolism where an excess of iron accumulates in the tissues particu larly of the reticulo endothelial system There is normally a controlled absorption of iron from the intestine so that greater amounts are accepted by the body when required as in anaemia There is probably a failure of this mechanism in haemo chromatosis so that over the years a vast quantity of iron—from 30 to 60 g—accumulates in the tissues (The normal quantity by contrast is approximately 4 g) This results in irritation and fibrosis of the liver and pancreas follows

Clinical Picture It occurs mainly in men and is rare before 20 years and usually presents in middle life as portal cirrhosis The presence of skin pig mentation and diabetes mellitus strongly suggests the diagnosis which is confirmed by a raised serum iron with an increased saturation of the iron bind ing capacity and the finding of iron in a skin and liver biopsy Treatment is symptomatic The only way to remove iron from the body is by phle botomy and improvement has been reported from regular venesection

Haemosiderosis is seen following repeated blood transfusion for aplastic anaemia and similar con ditions It is not known whether the typical picture of haemochromatosis with fine hepatic cirrhosis can result from this

The Pancreas

The pancreas is a dual organ The externally secret ing alveolar tissue forms pancreatic juice and the islets of Langerhans form an internal secretion The pancreatic juice is a clear alkaline fluid containing sodium bicarbonate and three main enzymes tryp sinogen the protein ferment which is normally activated by the enterokinase of intestinal secretions lipase a fat ferment and diastase or amylopsin a starch ferment About one litre of pancreatic juice is secreted daily and the flow is regulated by a hor monal mechanism Contact of acid and food with the upper intestinal mucosa probably releases from the mucosal cells secretin and pancreozymin Se cretin produces a large volume of juice of consider able alkalinity but low in enzymes whereas pancreozymin increases the output of enzymes Nervous control may be exercised as well by the vagus but its role is obscure Lack of pancreatic juice results in undigested food appearing in the stools and this is usually associated with diarrhoea The stools are light in colour bulky and oily due to the steatorrhoea from excessive fat Normally up to 7 g of fat is excreted in the stools every 24 hr this is mainly as split fat In pancreatic diseases the output in 24 hr may be increased to 20 g It would be expected that this would be in the form of neutral or unsplit fat and globules of such fat particles are often seen microscopically yet this is not invariable for the small intestine juices contain fat splitting enzymes and changes may occur from bacteria Thus reliance should not be placed upon relative proportions of split and unsplit fat, but rather on the total output of fat The la k of trypsin results in increased nitrogen in the stools (azotorrhoea) such as 6 g instead of the normal 1 to 2 g in 24 hr often striated meat fibres can be seen microscopically in the stool The internal secretion of the pancreas is insulin from the is' ts of Langerhans this tissue may be partially or com pletely destroyed in various diseases of the pancreas diabetes resulting Total pancreatectomy in humans is quite compatible with life it results in a fatty diarrhoea with malnutrition which can be con trolled with pancreatic extracts and diabetes It is curious that this diabetes may not be severe and require only about 40 units of insulin daily

Tests for Pancreatic Disease

1 The presence of steatorrhoea is looked for by estimating the daily output of fat over a period of three or more days

2 Microscopical examination of the stool may show oily globules of neutral fat or striated meat fibres

3 A glucose tolerance test may be of a diabetic type from damage to the islets of Langerhans

4 A plain X ray of the abdomen may show cal cification in the pancreas This is usually the result of pancreatitis

5 Duodenal intubation and aspiration of the pancreatic juice for analysis of its enzyme content Secretin as a stimulant of pancreatic juice can be

injected intravenously This test is more of a research procedure and is particularly used to distinguish idiopathic steatorrhoea from pancreatic steatorrhoea

6 Estimation of serum or urinary diastase (amylase) Diastase is formed in the liver reaches the pancreas in the blood and is then secreted in the pancreatic juice In acute pancreatitis there is a great rise in the blood level—up to 1 000 units from the normal upper limit of 200 units—and this is shortly followed by a high excretion in the urine—up to 400 units from the normal upper limit of 50 units This is a most valuable test of acute pancreatic lesions and may be used as a screening test for abdominal emergencies It may also be of help in the diagnosis of the painful upper abdominal episodes of a relapsing type of pancreatitis a serum amylase done during the attack of pain may show a transient rise above the normal

Pancreatitis

Aetiology Pancreatitis can be produced by organisms like the virus of mumps and perhaps other viruses as well Many cases are associated with biliary tract disease and gall stones Of considerable interest are the lesions due to auto-digestion of the pancreas The pancreatic juice is innocuous until activated this is normally done by the enterokinase of intestinal juice but also can be effected by bile by the kinase present in injured tissues of the pancreas (as may happen from surgical injury) and by the action of bacteria If such activation occurs in the gland itself digestion takes place with catastrophic consequence—giving acute haemorrhagic pancreatitis The origin of many cases is thought to be some obstruction at the sphincter of Oddi from a gall stone or from spasm this could result in a regurgitation of bile up the pancreatic duct with activation of its secretions and such a lesion can be produced experimentally by injection of bile or duodenal contents into Wirsungs duct There is as in the disease in man firstly a haemorrhagic necrosis from autolysis of the blood vessels and pancreatic cells next the pancreatic juice liberated by necrosis meets fat of its own and other neighbouring tissues and by its lipase produces fat necrosis this may appear as white opaque areas in the pancreas mesentery omentum and abdominal fat The rarity of acute haemorrhagic pancreatitis may be due to the fact that a stone in the ampulla blocks one or both ducts in the majority of cases and the anatomical fact that in 90 per cent of people the two main pancreatic ducts—Wirsungs main duct opening into the common bile duct in the ampulla of Vater and Santorini s accessory duct opening independently into the duodenum—are connected and offer an alternative path which prevents obstruction and damming back of the secretions Many cases of such acute autolytic lesions of the pancreas are unassociated with gall stones and spasm of the sphincter has been invoked as a cause of raised pressure in the pancreatic ducts This might explain the occurrence of the disease a few hours after a heavy meal associated with alcohol when pancreatic secretion is at its height It is also postulated that vascular lesions such as thrombosis might start off the autolytic process It seems that while auto-digestion is a fact that explains the pathological appearances the exact explanation of why it occurs in some lesions and not in others is unknown

Acute Pancreatitis

Patients with this condition present as acute abdominal emergencies with severe upper abdominal pain that may simulate a perforated ulcer There may be copious vomiting Shock and collapse occur early and the temperature may be subnormal but is often raised later There is epigastric tenderness with guarding the bluish discoloration of the flanks and slate blue colour of the umbilicus perhaps due to extravasated blood from peptic digestion are unusual but specific signs Diagnosis is difficult and often first made at laparotomy This may be unavoidable but better results are obtained from conservative treatment so that every effort should be made to establish a preoperative diagnosis The raised serum amylase is diagnostic it may show striking elevations within an hour or two after the onset of the attack or may take eight hours to rise to such levels and returns to normal in 2 or 3 days The urinary amylase is similarly of diagnostic value but the rise lags behind the serum level A leucocytosis of 20 000 or more is expected. Radiologically a segmental ileus involving the stomach small intestine or colon may be seen The first requisite of treatment is relief of pain Morphia or pethidine are usually necessary Both drugs unfortunately cause spasm of the sphincter of Oddi but this may be counteracted by prescribing glyceryl trinitrate at hourly intervals as well. On theoretical grounds it seems likely that resting the pancreas by avoiding stimuli to its secretion will improve the outlook These stimuli are provided by the contact of food or gastric juice with the walls of the duodenum which release the hormones controlling its function therefore nothing should be given by mouth and there should be continuous aspiration of the stomach juices by a stomach tube Shock will be dealt with along the usual lines Broad spectrum antibiotics may be used to control secondary infection Complications are tetany from the combination of large amounts of

calcium with fatty acids in the area of fat necrosis and the later development of a pseudo cyst from encapsulation of necrotic debris and haemorrhagic exudate The prognosis bears a direct relation to the severity of the pathological process when extensive degrees of necrosis occur, the mortality has been reported as 30 per cent or higher But there are undoubtedly many milder cases that survive and some may escape diagnosis

Chronic Pancreatitis

This is a disease that may be more common in practice than realized and it is not infrequently an unexpected finding at autopsy not having been diagnosed during life The pathological process varies from enlargement of the gland with induration and nodularity in the early stages to extreme degrees of atrophy where there may be little more remaining than a short fibrous cord Diagnosis is difficult because of the inaccessible site of the pancreas and the unsatisfactory nature of the tests of its function Little is known concerning the aetiology or natural history of the various types of chronic pancreatitis Many cases are associated with chronic inflammations of the biliary tract and a cholecystogram will show a diseased gall bladder Occasionally the pancreatitis is started by penetration of a duodenal ulcer Rare causes are haemochromatosis and fibrosis from malnutrition such as in ulcerative colitis Chronic pancreatitis is commonest in males in the fifth or sixth decade

Clinical Syndromes The following clinical syndromes may be recognized—

1 *Episodes of Upper Abdominal Pain* Some cases of pancreatitis may be symptomless others may cause a single attack or occasional attacks of epigastric discomfort a group gives rise to severe and disabling episodes of pain which has been termed chronic relapsing pancreatitis The attacks may simulate peptic ulcer in being relatively brief at the start then becoming longer until the pain is more or less continuous yet spontaneous termination of the pain may occur when the pancreas is completely atrophied without any acinar tissue The characteristics of the pain are not specific except that it may be aggravated by sitting up and leaning forward The most important of the pancreatic function tests is the serum amylase which should be done during a bout of pain Treatment is difficult Occasionally alcohol which causes spasm of the sphincter of Oddi is found to precipitate attacks and can be avoided Usually no cause is known to initiate the episodes and prophylaxis is impossible Analgesic drugs have to be prescribed Surgery as indicated by the numerous and different operations which have been suggested for the condition is of doubtful value Removal of associated gall stones makes little difference to the pancreatitis once it is established Currently division of the sphincter of Oddi is practised Sympathetic denervation of the upper abdomen will relieve pain and can be used in severe cases Total or sub total pancreatectomy has a high mortality rate and it is too early to assess the results by follow up studies

2 *Persistent Diarrhoea* Steatorrhoea should be excluded by a fat balance or estimation of the daily output of faecal fat in every case of unexplained chronic diarrhoea Pancreatitis can result in a painless steatorrhoea and is differentiated from other causes of steatorrhoea by duodenal intubation and estimation of the pancreatic enzymes as well as by the microscopical appearances of the stool The other pancreatic function tests may also help in establishing the diagnosis The treatment is by some effective pancreatic extract this should be taken during the meal in order to give it the best chance of avoiding destruction by the low pH of the stomach contents

3 *Jaundice* Involvement of the head of the pancreas by the fibrosing process can occlude the duct and give attacks of jaundice these may be associated with upper abdominal pain Rarely a picture of a painless progressive jaundice may simulate carcinoma of the head of the pancreas It may be impossible to distinguish the two at laparotomy and even biopsy may sometimes be doubtful A short circuit operation should be done if the jaundice is persistent

4 *Diabetes Mellitus* This is usually mild and the treatment does not differ from diabetes where there is no macroscopic lesion of the pancreas

5 *As a Cause of the Post cholecystectomy Syndrome* A diseased gall bladder is removed and attacks similar to gall bladder colic develop Cholecystitis and pancreatitis are frequently associated and some disorder of the pancreas should always be considered in these cases

6 *Incidental Discovery of a Large Abdominal Mass* This may be due to a cyst of the pancreas associated with pancreatitis It may be symptomless apart from pressure on adjacent organs Treatment is surgical

Cysts and Calculi of the Pancreas

Cysts are rarely of developmental origin The usual type are pseudo-cysts complicating acute or chronic pancreatitis these are due to encapsulation of necrotic debris or haemorrhagic exudate have no epithelial lining and are adherent to surrounding structures Others are retention cysts from obstruction of a pancreatic duct which have no epithelial lining and contain pancreatic secretions

Symptoms may be due to the underlying pancreatitis or to pressure on surrounding organs The treatment is surgery this may be simple but can also require all the surgeon s ingenuity complete excision may be too risky and measures such as tube drainage external marsupialization with the abdominal wall or internal drainage by an anastomosis between the cyst and the alimentary tract may be required Pancreaticolithiasis may involve the parenchyma but sometimes calculi form within the ducts both conditions are associated with pancreatitis and diagnosed radiologically by plain antero posterior and lateral films of the abdomen Pancreatic calculi can give colic It is not usually practicable to consider their removal by surgery

Fibrocystic disease of the pancreas is a congenital disorder where cystic changes in the pancreatic ducts are associated with cystic changes in the lungs It may be due to some change in the mucus which is more viscid than usual The infants may die at birth or survive to childhood when they show malnutrition and other changes from a fatty diarrhoea and suffer from chronic lung disease with bronchiectasis and fibrosis

Benign Tumours

Cystadenomas are true proliferative neoplasms arising from the pancreatic parenchyma and are rare Islet cell tumours are also rare but more important clinically as a treatable cause of hypoglycaemia (*see* p 147) They are frequently benign adenomas and if single can be removed

Carcinoma

Malignant disease of the pancreas involves those in late middle life it is commoner in men than women (2 1) Nothing is known concerning its aetiology Arising from the ducts or glandular tissue it may appear in any part of the pancreas but is more frequent in the head The scirrhous growths may remain localized to the gland and resemble a fibrosing pancreatitis metastases occur in the neighbouring glands or porta hepatis

Clinical Picture The classical onset of carcinoma of the pancreas is a painless progressive jaundice due to a growth in the head causing obstruction to the bile duct This causes back pressure of bile in the liver and much enlargement of that organ the increased pressure in the biliary system results in great distension of the gall bladder if it has not been fibrosed from previous inflammation Obstruction is supported by the patient s story of clay coloured stools and dark urine The jaundice gradually deepens to a yellow green colour and there is troublesome pruritus The patient wastes and after 6 or 12 months a mass may become palpable in the upper abdomen In the final stages local invasion of the duodenum may cause obstruction or similar blocking of the inferior vena cava may give oedema of both legs deposits may be felt in the liver and ascites may develop from peritoneal deposits

There are however variations on this typical picture Fluctuations in the jaundice can occur perhaps when the bile duct obstruction is due to oedema in the neighbourhood of the growth or if necrosis alters the local mechanics Similarly the jaundice may not be painless and indeed some have recorded pain particularly in the back in more than half the cases The nearer the growth is to the ampulla of Vater the sooner does jaundice occur and the earlier is the carcinoma discovered Lesions arising in the body or tail of the pancreas may therefore be most difficult to diagnose vague upper abdominal discomfort or pain together with other dyspeptic symptoms may be quite non specific and elude discovery until the appearance of a mass There is no jaundice or steatorrhoea Diabetes is rare even when the whole organ is replaced macroscopically by growth

Diagnosis The clinical picture with obstructive jaundice is usually fairly definite An enlarged liver with a distended palpable gall bladder (Courvoisier s Law) is almost pathognomonic The gall bladder is unlikely to be distended with the rare painless gall stone as it has become shrunken and fibrosed from previous cholecystitis the same applies to chronic pancreatitis for this is often associated with gall bladder disease The stools are pale and fatty from the absence of bile and pancreatic juice the urine contains bile and bile salts but with biliary obstruction is free from urobilin as no bile reaches or is absorbed from the intestine

Positive occult blood tests on the stools may indicate a carcinoma of the ampulla of Vater and it may be seen on barium X rays of the duodenum Cholecystography is useless if the serum bilirubin is much above 3 mg per cent Infective hepatitis may sometimes mimic carcinoma of the head of the pancreas but the liver is usually smaller than in extrahepatic biliary obstruction liver function tests should be done and occasionally liver biopsy may avoid a laparotomy and be less hazardous (if done by someone experienced in this procedure) A growth of the common bile duct is distinguished only at laparotomy

Treatment The treatment of obstructive jaundice is surgery and time should not be wasted in unnecessary investigations of doubtful value The hazards from bleeding are eliminated by preliminary injections of vitamin K which corrects the prolonged prothrombin time due to defective absorp

tion of vitamin K. If the cause is stone, the stone can be removed If the cause is tumour the jaundice can be alleviated by a short circuit operation If the obstruction is due to some other cause it is seldom possible to be confident enough of a clini cal diagnosis to refuse the patient the hope that operation offers It may be possible at operation to distinguish between carcinoma of the pancreas and chronic pancreatitis and indeed there may be an obstructive atrophic lesion of the pancreas from obstruction from a carcinoma of the main duct. A cholecyst-enterostomy relieves the jaundice with its intolerable itching Occasionally a growth can be removed by a sub total pancreatectomy Total pancreatectomy is occasionally performed it is hazardous and the follow up results are not good

REFERENCE

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CHAPTER 15

Diseases of the Cardiovascular System

WILLIAM E CLARKE

Heart Disease

HEART disease is the most common cause of death and its incidence is increasing Some of this increase is due to the control of infectious disease and the increasing age of the population but apart from this coronary artery disease and hypertension are becoming more prevalent and affecting younger age groups Rheumatic heart disease the third large aetiological group is slowly decreasing due possibly to improvement in general social conditions Syphilitic heart disease is also diminishing with better education and control of this infection The incidence of other groups remains much the same The importance of recognizing those due to mechanical defects such as congenital and chronic rheumatic lesions must be stressed with the increasing ability of the thoracic surgeon to rectify such conditions Precision in diagnosis is aided by the judicious use of old and new methods of investigation The history and clinical examination must however remain the most important methods These with radiology and electro-cardiography will generally be sufficient to give one the diagnosis The more complicated cases will need cardiac catheterization angiocardiography blood gas analysis and other procedures

The Patient s History This must be taken without hurry and if necessary alone By it one learns to know the man as well as his cardiac complaints Often his symptoms are a result of his psychological make up Indeed when a fearful person has precise knowledge of a complaint it may be impossible to rule out actual disease usually however discrepancies show themselves when he is questioned narrowly A careful history will give one the certain diagnosis of angina pectoris when every objective test is normal it will mark the progress of diminishing cardiac reserve better than any test and tell the onset of left ventricular failure with nocturnal paroxysms of dyspnoea and later the onset of right ventricular failure with easing of symptoms and the development of oedema Function may be assessed by the history but individual defects are recognized by clinical examination

The Examination

A general assessment of the patient s character is made while the history is being taken His build degree of overweight or wasting evidence of plethora or anaemia and the presence or absence of cyanosis is noted Orthopnoea may be present and short of this his sentences may be interrupted by quick taken breaths A description given in long easy sentences belies a history of dyspnoea despite frequent sighs and straining respirations The important cardiological factors to determine are—

1 The presence or absence of failure of the heart
2 The size of the heart
3 The rate and rhythm of the heart
4 The level of the blood pressure

Cardiovascular details are noted at the same time that a general examination is performed It is less distressing to an ill patient to be examined from head to feet than system by system In this way facts in the following order are observed—

Head and Neck The fundi will give evidence of normal vessels show arteriosclerosis with tortuous thickened vessels or hypertensive changes with narrowed arteries exudates and haemorrhages with or without papilloedema Emboli are seen anaemia noted and evidence of other disease found Papill oedema with engorged veins is also seen in emphysema when slight oedema of the conjunctivae is also present The eyes are bright quick moving and may be proptotic in thyrotoxicosis When central cyanosis is present it can be seen in the tongue and palate as well as the lips With a high arched aorta the right common carotid artery may be raised and kinked simulating an aneurysm The arteries may be pulsating over vigorously—the Corrigan pulse of aortic regurgitation By far the most important physical sign in the neck is the presence or absence of over filling of the veins with the patient reclining at 45 They may be distended to the angle of the jaw moving the lobe of the ear if less filled pulsation is seen at their upper level

tion of vitamin K If the cause is stone the stone can be removed If the cause is tumour the jaundice can be alleviated by a short circuit operation If the obstruction is due to some other cause it is seldom possible to be confident enough of a clinical diagnosis to refuse the patient the hope that operation offers It may be possible at operation to distinguish between carcinoma of the pancreas and chronic pancreatitis and indeed there may be an obstructive atrophic lesion of the pancreas from obstruction from a carcinoma of the main duct A cholecyst-enterostomy relieves the jaundice with its intolerable itching Occasionally a growth can be removed by a sub total pancreatectomy Total pancreatectomy is occasionally performed it is hazardous and the follow up results are not good

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place The sudden falling away of the pulse wave is due to peripheral vaso dilatation and reflux of blood into the left ventricle It is also found in conditions of general vaso dilatation without aortic regurgitation

Pulsus alternans is of serious import and indicates a failing left ventricle The heart beats are of alternating force a weak beat succeeding a strong beat It varies in degree from differences of a few mm Hg to 20 mm or more Its mechanism is unknown

Pulsus paradoxus is present when the normal inflow of blood to the heart is impeded Ordinarily there may be a slight fall in blood pressure and increase in pulse rate with inspiration due to an increase in the volume of the pulmonary circulation In inspiration however the venous return is increased and may completely compensate for this increase in volume The blood flow to the left ventricle is therefore maintained and the cardiac output does not suffer When the systemic return is obstructed however as in adherent pericarditis or pericardial effusion this compensatory increase can not occur a marked fall in cardiac output and blood pressure results so that the pulse may even disappear entirely

The Blood Pressure

A mercury sphygmomanometer should be used as it is more reliable than the anaeroid machine The patient sits or lies as relaxed as he can manage with no restricting clothes between the cuff of the instrument and the axilla Time should be allowed for him to settle down after the effort of undressing and getting on to the couch The brachial artery is identified by palpation and the end piece of the stethoscope placed lightly on it any pressure interferes with the systolic and especially the diastolic reading The reading is taken slowly and slowly repeated in nervous patients the tightening arm band is enough to raise the blood pressure which falls to a level nearer the basal reading as he becomes acquainted with the exact sensations to be experienced In the first reading the pressure needed to obliterate the pulse is estimated by palpation at the wrist in the second reading the pressure is rais d well above this in any case it is taken above 200 mm Hg This is usually sufficient to avoid the silent gap The systolic pressure is defined as the level at which successive sounds are heard As the level falls the sounds become muffled and in hypertensive patients may disappear altogether to reappear at a lower level this is the silent gap The sounds then become clearer and louder suddenly to fall away and disappear over a small pressure range The level at which this occurs is the diastolic reading The pressure is lowered slowly at the upper level care is taken that pulsus alternans is not present At the lower level the pressure may fall away through a wide range The pressure of the stethoscope must be lightened but in peripheral vaso dilatation sounds may continue to zero

Examination of the Heart

Inspection The general shape of the chest and precordium and the presence of pulsation or retraction are noted and the latter timed against the heart beat and respiration When gross cardiac enlargement has been present from childhood bulging of the precordium over the affected chambers is present The apex beat is carefully sought and its position rhythm rate and character is noted Enlargement of the heart of any degree denotes cardiac pathology and it is of the first importance to decide whether or not such enlargement is present A normal heart may be displaced by factors enumerated under examination of the chest Pulsation over the pulmonary outflow tract in the second and third left intercostal spaces indicates pulmonary hypertension and is usually accompanied by pulsation of the right ventricle in the epigastrium Pulsation in the right second interspace near the sternum is caused by an aneurysm of the ascending aorta Retraction of the lower left ribs posteriorly is seen in adherent pericardium (Broadbent s Sign)

Palpation This gives more precise information about the apex beat which may be described as the most downward and outward point at which a definite lift may be felt with systole When no apex beat is seen the palm of the hand is placed on the lateral chest wall and brought round towards the midline anteriorly This prevents one overlooking a very large failing heart with a poor apex beat and gallop rhythm if gallop rhythm is also present a deceptive impulse may be felt nearer the midline than the actual apex beat Once the general area of pulsation is determined the precise apex beat is located by placing the index or middle finger tip against the chest wall and seeing and feeling its movement The normal position is – in within the midclavicular line in the fifth intercostal space It may be of poor force and diffuse sharp and tapping or slow rising and lifting The forceful heaving beat of the hypertrophied left ventricle is due to the firmly contracted myocardium being forced against the chest wall by the uncoiling of the aorta during systole when the aorta is made to straighten out by the steep rise in pressure within it If failure develops and the systolic pressure falls this quality is lost although the heart is still grossly enlarged and dilated Thrills are located and their timing in systole or diastole determined Taken in conjunction

the exact rhythm is examined by a venous tracing which gives valuable information about the heart rhythm

Upper Limbs The arms are examined for wasting the condition of the brachial artery the pulse and the estimation of the blood pressure The fingers are inspected for tremor and the nails for clubbing koilonychia and splinter haemorrhages The *pulse* and *blood pressure estimation* are described later

Chest Examination of the chest may reveal emphysema or asthma whose symptoms may be mistaken for those of diminishing cardiac reserve Their presence does not exclude heart disease Crepitations at the lung bases or pleural effusions occur with left and right ventricular failure Pleural effusion or pneumothorax fibrosis or collapse of the lung and scoliosis and depression of the sternum may cause displacement of the heart Examination *of the heart will be described later*

Abdomen In the abdomen a positive hepato jugular reflex indicates failing right ventricular reserve An enlarged liver is present in right ventricular failure It is best felt in the epigastric notch where it causes a visible fullness and dullness to percussion It is tender if the enlargement has been rapid It is less easily felt below the right costal margin where its lower border may be mistaken for an intersection of the rectus abdominis or *vice versa* Pulsation may be seen and felt if tricuspid *regurgitation is present* When ascites is present the size of the liver may have to be determined by ballottement The abdominal aorta is often felt and *may be tortuous or even aneurysmal*

Lower Limbs In the lower limbs the condition of the peripheral vessels is determined at the femoral popliteal posterior tibial and dorsalis pedis vessels In about 10 per cent of cases the dorsalis pedis arteries are developmentally small or absent Pulsation in the femoral arteries is poor in the presence of coarctation of the aorta and so this must be carefully assessed in all cases of hypertension Oedema is sought the earliest signs being found behind the ankles and thighs in patients confined to bed Thumb pressure is maintained for at least half a minute in doubtful cases to determine the presence of pitting When gross the swelling *spreads up the thighs* to affect the genitals and lumbo sacral region When very gross the skin is stretched and pale it may ooze fluid and sub *acute cellulitic areas* develop

The Pulse

This is felt at both *wrists simultaneously* any difference in quality leading to estimation of the blood pressure in both arms and a search for extra and intra thoracic causes for such a difference The pulse rate its rhythm volum tension and the state of the artery wall are judged When the rate is slow or the rhythm irregular simultaneous auscultation at the apex must be carried out A *pulse deficit may thus be discovered that is a difference* in rate of the heart at the apex and of the pulse at the wrist It helps to distinguish between extra *systoles and auricular fibrillation* although this may be impossible without instrumental aid It may show that a slow rate at the wrist is in fact due to a pulse deficit When one ventricular contraction follows closely on another the poorly filled ventricle contracts with insufficient force to open the aortic valve Then only a first sound is heard If the aortic valve is opened two heart sounds are present, but *the pulse may be too weak to reach the wrist*. In both these cases no pulse can be felt at the wrist due to the inadequate ventricular contraction

The Pulse Volume This is described as full and bounding or small depending on the force of expansion of the artery with each pulse wave It depends on the force of the heart action the blood volume and the state of the artery wall Thus hypertension hyperkinetic states or peripheral vasodilatation and thickened artery walls which cause an increase in the pulse pressure are associated with a full pulse Myocardial infarction haemorrhage or shock result in a small pulse

The Tension This is a measure of the blood *pressure* and *although interesting* to gauge it by digital pressure over the brachial artery it must be ascertained by the sphygmomanometer

The state of the artery wall is examined for thickness tortuosity or even calcification It is inspected at the brachial vessels and wrist and in the neck and the lower limbs

Special Characters of the Pulse Wave In the normal pulse tracing at the wrist the dicrotic notch occurs on the downstroke of the wave *the so-called* catacrotic tracing

An anacrotic pulse has the notch on the upstroke and is characteristic of aortic stenosis *The pulse is* late in arriving and slow rising

The pulsus bisferiens is a variation of the anacrotic pulse indicating combined stenosis and regurgitation The tidal wave and percussion wave are about equal and close together

When the dicrotic wave is increased it may be felt as a separate impulse thus being known as a dicrotic pulse It is found when arteriolar dilatation is marked and in aortic regurgitation

Corrigan s pulse characterizes aortic incompetence The pulse is bounding and rapidly rising but immediately following the sharp impact an equally rapid falling away of the pulse wave takes

It may be normal or indicate heart disease As stated earlier a third heart sound may be normal in children and young adults A pathological *proto diastolic triple rhythm* indicates serious myocardial damage and is believed to be produced by blood flowing into a dilated flabby ventricle If the left ventricle is mainly affected it is best heard at the apex if the right in the third and fourth left inter spaces near the sternum It is low pitched and follows the second sound after an appreciable pause as does the normal third heart sound When patho logical however the heart is enlarged there is a distinct impulse with the sound and there is other evidence of cardiac disease The history indicates a diminished reserve *In pre systolic triple rhythm* a similar sound occurs just before the first heart sound It also generally indicates left ventricular strain It is an audible auricular contraction with a prolonged P R interval As the heart rate rises and as the P R interval increases the protodiastolic sound (or third heart sound) and the pre systolic sound approach each other until they synchronize They then supplement each other and a summation gallop is produced The heart rate is as a rule raised over 100 per min then the rhythm approxi mates to that of a horse galloping It is not always possible exactly to time these sounds When the heart rate exceeds 100 per min the diastolic pause is less than 1/200th of a min as the speed rises the exact point in diastole becomes more difficult to determine

Cardiac Murmurs Having listened carefully to the heart sounds themselves added sounds the heart murmurs are listened to and their site propaga tion character and timing defined They are timed as systolic or diastolic the thumb being placed lightly on the carotid artery in the neck to decide the beginning of the systole Systolic murmurs have been classified as ejection murmurs when they begin in mid systole and regurgitant murmurs when they are pan systolic With regurgitant murmurs the pressure needed to open the mitral or tricuspid valves is less than that needed for the opening of the aortic or pulmonary valves and the murmurs therefore begin with systole

Diastolic murmurs may be timed precisely if the heart rate is not too fast and their point of maxi mum intensity and conduction determined They indicate regurgitation through an incompetent valve or orifice Some murmurs are continuous through systole and diastole and are due to arterio venous communications *e g* patent ductus arteriosus A V fistula or aortico pulmonary anastomosis

Apical systolic murmurs may be functional especially when they are heard only at the apex or between it and the sternum and vary with respira tion or position of the patient They may be con ducted from the aorta and are commonly found with atheroma of the aortic valve or with a dilated first part of the aorta Systolic murmurs from the pulmonary area are conducted to the base of the sternum

Apical diastolic murmurs usually indicate mitral stenosis but aortic regurgitant murmurs are often better heard at the apex than at the aorta With mitral stenosis there is a pause between the second sound and the onset of the murmur which begins with the third heart sound With aortic regurgita tion the murmur follows immediately after the second sound without this gap

Basal diastolic murmurs relate to aortic or pul monary regurgitation They are high pitched soft and blowing beginning with the second sound The second sound is usually not well marked when re gurgitation is free

A pericardial murmur or friction rub has a differ ent character it is more superficial grating or crunching and may have three periods of accentua tion in a cycle auricular systole ventricular systole and diastolic filling movement giving rise to a shuffling sound

Electrocardiography

This is an important aid in the assessment of any cardiological patient and in some cases is essential Stimulation and contraction of the heart muscle are accompanied by electrical changes which are con ducted by the body tissues to the surface These can be magnified and recorded the tracing being known as electrocardiogram The instrument used is either a string galvanometer or a system of valve ampli fiers The former is still the more sensitive and reliable but the latter affords convenient portable direct writing machines As technological advances make the taking of electrocardiograms easier multiple leads and increasing knowledge places a greater responsibility on the person interpreting the result Interpretation should be undertaken only with the full history and clinical findings alone the electrocardiogram can be most misleading

Electrocardiography indicates the time relation ship of the activity of auricles and ventricles and clarifies cardiac arrhythmias It gives a guide to the position of the heart in the chest and the rela tive size of the two ventricles It gives information about the state of the myocardium especially in flammatory ischaemic and metabolic disorders and the effects of various drugs and electrolytes It does not help in determining cardiac reserve or failure and does not help in assessing prognosis

The unipolar leads reflect the changes in electro motive force at certain points in the unipolar limb

with auscultory findings they help in deciding the nature and position of mechanical defects within and in the neighbourhood of the heart A thrill is caused by the rapid passage of blood through a narrow orifice and its intensity depends on the force of the heart beat and size of the aperture When the force diminishes the thrill tends to disappear The exact site and significance of thrills will be discussed under individual conditions

Percussion Percussion even in the most skilful hands does not necessarily give a reliable indication of the size of the heart when the chest is emphyse matous it may be very misleading However this method of assessment of heart size should be prac tised the results being compared whenever possible with radiological findings as a check This is neces sary as radiological help may not be available or it may be inadvisable to move the patient

Percussion may be of value when pericardial effusion is present the outer border in the second and third left interspaces moves outward when the patient lies down after sitting up It may be possible also to percuss solid tumours of the superior mediastinum and aortic aneurysms of the first part of the aorta

Auscultation Two normal heart sounds occur a normal third heart sound is heard in most young children and in some adolescents

The first heart sound is composite it is mainly due to closure of the mitral and tricuspid valves but residual auricular vibrations ventricular con traction the opening of the aortic and pulmonary valves and the acceleration of blood into the main vessels also contribute to it The character of the mitral and tricuspid valve flaps and their position at the onset of ventricular contraction largely deter mines the intensity of the first sound If the P R interval is short as in tachycardia if there is obstruction to the passage of blood from the auricles to the ventricles as in mitral stenosis or if the venous return is large as in exercise or certain shunts the valves will be held well down into the ventricles by the flow of blood until the onset of the next systole With systole they will be brought smartly together and be set in intense vibration A loud first sound results If the flaps are thickened rigid or calcified they are incapable of rapid large movements and a quiet first sound results If the P R interval is prolonged the valve flaps will have had time to float almost into apposition Then the first sound will be quiet despite a powerful left ventricle A poorly contracting myocardium with a normal P R interval may also result in a quiet first heart sound

The second heart sound is due to the closure of the pulmonary and aortic valves and the vibration of the great vessels at the end of systole It is usually single, but slight asynchrony of closure may nor mally occur with splitting of the second sound at the pulmonary area The second sound is accentuated when the pressure in the aorta or pulmonary artery is raised or the vessels dilated

The loudness of both heart sounds also depends on the proximity of the heart to the chest wall Thus in muscular fat or emphysematous patients, the sounds will be less intense than in thin patients or in those whose lungs are fibrosed and retracted from between the heart and the chest wall

The third heart sound is believed to be due to the rapid flow of blood into the ventricles in early diastole It follows the second sound after an appreciable interval is low in pitch and is best heard with the child lying on its left side and when the heart rate is slow Its intensity varies with respiration

Split or reduplicated sounds explain themselves Split first and second sounds may be normal and it is most important not to be misled by them into diagnosing valvular disease or pathological triple rhythm Any deviation from the normal in (1) con duction of the cardiac impulse or (2) contraction of muscle or (3) disturbance in pressure relationship in the aortic and pulmonary systems may cause separate components of one or other sounds to become recognizable as distinct entities and cause a split sound If the separation is more marked third or fourth heart sounds are produced

A split first sound may indicate bundle branch block usually of the right side A split second sound is normally heard at the pulmonary area the splitting being increased by deep inspiration The first element is aortic the second pulmonary A deep inspiration increases the venous filling of the right ventricle which takes longer to empty and tends to decrease the venous filling of the left ventricle which empties more quickly thus producing a greater asynchrony in the times of the contractions of the ventricles and the splitting becomes more obvious

Triple rhythm is present whenever 3 distinct heart sounds occur in each cardiac cycle (Fig 15 1)

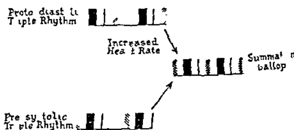


Fig 15 1 Cardiac Murmurs

leads the exploring electrode is placed on the right arm left arm and left leg respectively the other electrode being kept at zero potential A galvano meter placed between the two electrodes measures the electromotive force at the exploring electrode In the case of the chest leads the exploring elec trode is placed at agreed points over the chest wall (Fig 15 3) and measures the electrical changes in the horizontal plane The so-called standard leads

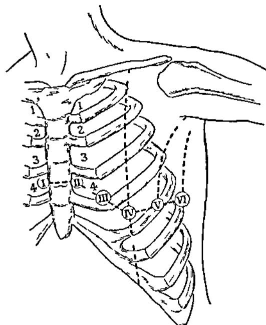


FIG 15 3 POSITIONS OF ELECTRODES IN TAKING PRE CONDIAL ELECTROCARDIOGRAMS

are bipolar and measure the difference between the unipolar potential thus lead 1 is the difference between the left arm and right arm potentials lead 2 that between the left leg and right arm potentials and lead 3 that between the left arm and left leg potentials (Fig 15 2)

The electrocardiogram should be examined systematically the heart rate is determined and arrhythmias recognized the electrical axis deter mined and the individual components of the tracing examined

The Heart Rate The tracing is taken on a paper already marked or the time marking is taken with the electrocardiogram Each small section equals 0 04 sec each large section 0 2 sec There are thus 300 large sections per minute if the number of large sections between two corresponding points on successive cycles is divided into 300 the result is the number of heart beats per minute

The rhythm is considered more fully later

The electrical axis is recognized by comparing the QRS complexes in various leads The instan taneous electrical axis is the resultant of all the electrical changes taking place in the heart muscle at one moment and has magnitude direction and sense The mean electrical axis of the QRS com plex is the algebraic sum of these changes while the impulse is invading the ventricles Its direction *gives the electrical axis of the heart It can be* resolved into components in various planes usually in the frontal plane and they are considered in leads 1 and 3 When the R wave in lead 1 and the S wave in lead 3 are the main deflexions left axis deviation is present when the S wave in lead 1 and the R wave in lead 3 are the main deflexions right axis deviation is present This is usually due to the horizontal or vertical position of the heart but may be added to by hypertrophy and preponderance of the left or right ventricular muscle

The P wave is produced by the spread of the excitation wave over the auricles Normally it is smoothly humped and does not last longer than 0 11 sec or exceed more than 2 mm in height. It is *tall and pointed in right ventricular hypertrophy or* strain *e g* acute or chronic cor pulmonale In left auricular hypertrophy it is broadened notched or M shaped It is absent in auricular fibrillation being replaced by minute rapid F waves

The P R interval measures the time taken for the impulse to pass from the auricles to the ventricles It is iso-electric but it may be depressed in its latter part by the recovery phase of the auricles It should not exceed 0 2 sec It is prolonged in rheumatic or diphtheritic myocarditis coronary artery disease and by digitalis therapy

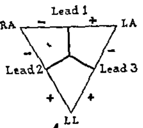
The QRS complex represents the electrical changes brought about by the invasion of the ven tricles by the excitation process It should not exceed 0 1 sec It gives information about the conducting tissue and the mode of spread of the impulse myo cardial hypertrophy the site of injury when present and the effects of potassium digitalis and quinidine The S T segment and T wave represents the iso electric phase and repolarization of the ventricles It too is affected by hypertrophy of the ventricles potassium and digitalis It is also altered by is chaemia injury and inflammation Fig 15 4 shows a normal electrocardiogram

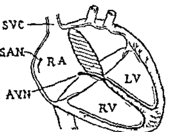
Radiology

Radiology is a very valuable part of the cardio vascular assessment of a patient. Various techniques have been developed each giving specific informa tion

Fluoroscopy entails the direct viewing of the chest

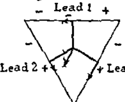
Einthoven's Triangle



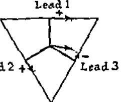


The Conducting System of the Heart

Right Axis Deviation

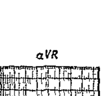


Left Axis Deviation

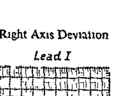


Right Axis Deviation

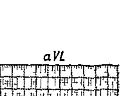
aVR



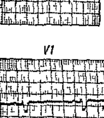
Lead I



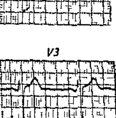
aVL



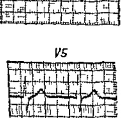
V1



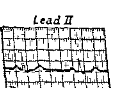
V3



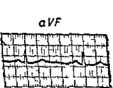
V5



Lead II



aVF

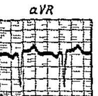


Lead III

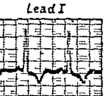


Left Axis Deviation

aVR



Lead I

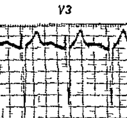


aVL

V1

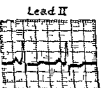


V3

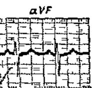


V5

Lead II



aVF



Lead III

Fig 15 2 Einthoven's Triangle with below ECGs Pertaining to Right and Left Axis Deviation

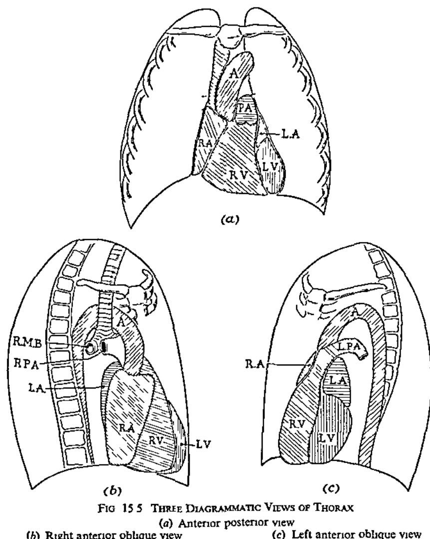


FIG 15 5 THREE DIAGRAMMATIC VIEWS OF THORAX
(a) Anterior posterior view
(b) Right anterior oblique view (c) Left anterior oblique view

Phonocardiography by this means heart sounds are recorded graphically It has been of value in analysing the heart sounds and clinically is of help in determining the precise time and quality of a heart-sound and murmur Tape recordings may be made and played back for teaching purposes

Ballistocardiography the contraction of the heart and the passage of the blood along the great vessels during a cardiac cycle transmit forces of varying degree and direction to the body as a whole These may be picked up usually only those components of the total that act in a longitudinal direction and may be magnified and reproduced as a continuous tracing These may be analysed and correlated with known changes in the cardiac cycle in healthy and pathological hearts This method of examination is still in an experimental stage and is not in routine use

The Cardiac Arrhythmias

The heart is stimulated to beat normally by impulses which arise in the junctional or neuromuscular tissue The inherent rhythm of the sino auricular node is more rapid than that of the auric ulo ventricular node which in turn is faster than that of the Bundle of His or its branches. Thus the

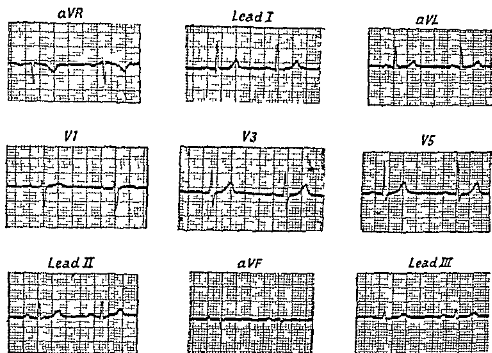


FIG 15 4 A NORMAL ELECTROCARDIOGRAM (HORIZONTAL LIE)

and heart on a fluorescent screen The shape and size of the heart relative to the thoracic cage is seen and the relative size of the individual chambers and great vessels with their degree of movement in systole and diastole Pericardial effusions can be made out and any calcification in the valves or pericardium located By rotating the patient while observing the heart the heart size shape and action in three dimensions is seen (Fig 15 5) These measurements are relative as the proximity of the tube to the screen magnifies the image By swallowing a barium emulsion the posterior surface of the heart is outlined Abnormalities in oesophageal contraction or mediastinal masses are discerned The pulmonary vasculature the lung parenchyma and diaphragmatic movement are observed Pleural effusions are seen when small these may not be found on clinical examination The various parts of the heart seen in the three standard views are shown in Fig 15 5 Plate 15 1 is a chest X ray which shows a normal heart outline

A teleradiogram approximates more nearly to actual measurements This is a film taken by a tube 6 ft away from the screen the rays are then nearer parallel these are taken for record purposes as well as immediate inspection

An orthodiagram gives the preci e heart size it is taken by following the thoracic and heart outline with a moving beam at right angles to the screen The screen is stationary the X ray tube moves and the grid aperture is cut down to a small size A permanent record is obtained by using a pencil on a transparent sheet of paper on the viewing screen The degree of added accuracy is small however is time consuming and when inexpertly done the patient is exposed to lengthy irradiation during an examination in which errors can be made in the results

Angiocardiography outlines the individual chambers of the heart by means of a radio-opaque medium injected into the cephalic vein or the superior vena cava It is a valuable method of investigation especially in difficult congenital heart lesions It may be combined with cine radiography in which a specially synchronized camera takes a moving photograph of the medium as it traverses the heart and great vessels

Cardiac catheterization is still used mainly in research but is of value clinically in elucidating certain congenital shunts and in acquired heart disease such as mitral stenosis and pulmonary hypertension A fine radio opaque catheter is passed into the antecubital vein and pushed into the right auricle right ventricle and the pulmonary artery as far as its smaller branches It may be passed through intra auricular or intraventricular defects into the left side of the heart and so into the aorta Pressure changes are recorded and blood samples taken Their gas content is analysed and so the degree of any shunt present can be determined

inanition and depressive states Drugs especially digitalis and quinidine produce it It is induced mechanically by carotid sinus pressure There are usually no symptoms The pulse pressure is high and the diastolic pressure usually low On screening the ventricles are enlarged at the end of the long diastolic filling and the ventricles may also become hypertrophied

Tachycardia Any rate more rapid than 100/min is described as tachycardia (Fig 15 9) It is normally

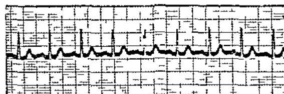


FIG 15 9 SINUS TACHYCARDIA (V6)

found in children when found in adults a cause should be sought but it may be found without organic disease It is produced by exercise or emotion especially excitement or fear and in thyrotoxicosis It is found in acute infections or the toxaemia of chronic illnesses A fall in blood pressure as with shock or haemorrhage or a rise in pressure in the great veins and right auricle as in heart failure or in hyperkinitic states result in reflex tachycardia Tachycardia is the only means of maintaining the cardiac output in constrictive pericarditis or pericardial effusion In neuro circulatory asthenia the heart rate is maintained well above 100/min but this may fall during sleep to normal Drugs affecting the sympathetic or parasympathetic systems such as adrenaline atropine and amyl nitrite or tea coffee alcohol and smoking can produce it It may result in palpitations but is often symptomless No treatm nt is needed except that directed to the exciting cause

Sino atrial Block (Sinus Arrest) This results from increased vagal activity and may be due to digitalis quinidine or potassium administration It may occur with an over sensitive carotid sinus. It results in a completely inactive heart for one or more beats When the pause is short no symptoms occur when prolonged the cardiac arrest causes faintness and nervousness similar to Stokes Adams attacks due to ventricular arrest It is diagnosed by electro cardiography (Fig 15 14 (*a*))

If the attacks are due to an over active carotid sinus and are frequent and troublesome the sinus may be denervated If less troublesome tinct belladonna 1 ml (15 minims) t d s ephedrine 30 mg (½ gr) t d s and a sedative may be given Cessation of the causative drug is often sufficient to bring about a cure

Auricular Ectopic Rhythms

Auricular extrasystoles (Fig 15 10) auricular tachycardia flutter and fibrillation may be grouped together as the heart beat originates at an ectopic focus in the auricular muscle Each however presents a distinct clinical entity

Auricular Premature Contractions (Auricular Extra systoles)

An aberrant irritable focus in the auricle initiates a contraction before the next sino auricular stimulus occurs Its site and the abnormal spread of stimulus over the auricle causes an abnormal P wave If the ectopic beat is very premature the auriculo ventricular node is still refractory and the impulse does not reach the ventricles such an occurrence is recognized only by electrocardiography Usually conduction occurs and the ventricles contract prematurely if very soon after the previous beat the ventricles contain a small amount of returned blood and the force of contraction is correspondingly poor It may be insufficient to open the aortic valves In this case only the first sound is heard on auscultation at the apex

The longer the interval the more blood will have returned to the ventricles and the nearer will the premature beat approach a normal beat in time

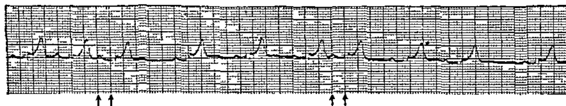


FIG 15 10 AURICULAR EXTRASYSTOLES
The P R interval is prolonged in the beats between the arrows

sino auricular node lying in the sulcus between the superior vena cava and the free border of the right auricular appendage as it enters the right auricle controls the heart rate and is therefore known as the pacemaker Its rate is determined by the balance between stimuli from the vagus and sympathetic nerves which control it—usually about 70/min It may vary between 40 and 100/min in health The impulse spreads over the auricles in all directions to reach the auriculo ventricular node by which it is conducted to the ventricles Should the auricular rate fall below that of the intrinsic rhythm of this structure the heart rate is controlled by the auriculo ventricular node The impulse then spreads simultaneously to the auricles and ventricles the rhythm being called nodal rhythm The impulse is carried to the Bundle of His this soon divides into right and left branches which pass to the right and left ventricles respectively These bundles divide into progressively smaller branches to end in the fine network of Purkinje fibres lying under the endocardium These stimulate the heart muscle to contract the impulse spreading outwards through the muscle from the endocardium towards the pericardium Further slowing of the heart causes the idio ventricular pacemaker to control the heart rate This is placed farther down the Bundle of His but before its bifurcation so that the electrocardiogram is of a supraventricular pattern The rhythmicity here is usually below 40/min

Sinus Rhythm This term is used to describe the normal beating of the heart the impulse arising in the sino auricular node and spreading in the manner described above to result in a contraction of the ventricles It implies that the rhythm clinically is completely regular

Sinus Arrhythmia (Fig 15 7) Even in sinus rhythm a slight waxing and waning of rate occurs. When this is easily recognized it is called sinus arrhythmia It is caused by variations in vagal tone produced from alveolar stimuli during respiration In inspiration, the heart rate increases in expiration

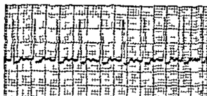


FIG 15 6 PAROXYSMAL TACHYCARDIA
Note inverted P

it slows After a deep breath this slowing may be extreme and unless the cause is recognized the condition may be mistaken for intermittent sinus block or auricular fibrillation It is of no pathological significance, and is most commonly found in childhood adolescence and in old age It is increased by any condition increasing vagal tone and so is seen in bradycardia and during digitalis medication

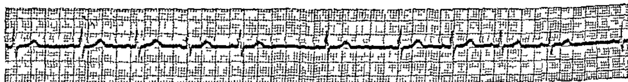


FIG 15 7 SINUS ARRHYTHMIA

Bradycardia When the heart rate is below 60/min bradycardia is said to be present In sinus bradycardia (Fig 15 8) the origin and spread of the stimulus is normal It is seen in athletes and in normal people with a pronounced vagal tone It sometimes occurs during sleep It is characteristically found in myxoedema and in rapid rise in intracranial pressure It is associated with convalescence from infectious fevers and influenza with jaundice

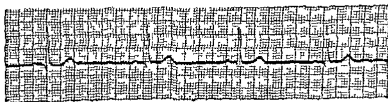


FIG 15 8 SINUS BRADYCARDIA (AVL)

by its unvarying rate which is not affected by exercise respiration or carotid sinus pressure. The onset and offset of sinus tachycardia are gradual and the rate is as a rule lower than in paroxysmal tachycardia In auricular flutter the auricular rate is usually 240–260/min the ventricles beating at 60–90/min or 120–180 min depending on the degree of heart block Then exercise may suddenly double the rate or carotid sinus pressure may suddenly halve the rate the heart equally abruptly reverting to its former rate when the exercise or pressure ceases In uncontrolled auricular fibrillation the heart rate is completely irregular and usually quite fast 160–180/min exercise increases the irregularity and the rate and carotid sinus pressure produces little change

Treatment If the patient has had the condition for some time he has usually discovered some means of cutting short the attack. The commonest are compression of the abdomen breath holding in deep inspiration drinking cold water or inducing vomiting Other methods often successful are compression of one carotid sinus against the transverse process of the 7th cervical vertebra trying the right first, or compression of the eye balls the patient looking downwards with the eyes closed If the attack continues acetyl beta methylcholine (Mecholyl) 10–20 mg intramuscularly or prostigmine 1–2 mg intramuscularly are given to stimulate the vagus Unpleasant side effects of these drugs include flushing sweating abdominal colic sudden micturition and defaecation bronchospasm urticaria and prolonged sinus arrest. Atropine sulphate 1 0 mg should be drawn up in a syringe ready for administration in case they occur If these measures are ineffective digoxin 1 0 mg is given intravenously provided no digitalis had been administered in the previous three weeks This may be given before the cholinergic drugs it often succeeds when they fail. Carotid sinus stimulation may again be tried after these drugs have been given it may then stop the attack Lastly quinidine may be given by mouth or intramuscularly 2 hr after a test dose of 0 2 g (3 gr) 0 4 g (6 gr) is given 2 hourly for 6 to 8 doses or until sinus rhythm is restored

After the attack has ceased quinidine 0 4 g (6 gr) may be continued t d s together with potassium bromide if the attacks had been frequent, as this tends to diminish their incidence As a rule they are so unpredictable that continuous preventive treatment is not indicated

Auricular Flutter (Fig 15 11)

In flutter the auricles are beating regularly at between 260 and 360/min the A V node is unable to respond at this rate so that there is a 2 1 3 1 or 4 1 heart block present The ventricles therefore beat at roughly 180 120 or 80/min When the degree of heart block varies rhythm is irregular The rate is usually completely regular however and is not affected by effort emotion posture or breathing

Aetiology It occurs more commonly in men than in women and usually in the older age groups but no age is exempt. Rarely the heart is normal but in most cases it is associated with mitral stenosis coronary artery disease or cardiac infarction thyrotoxicosis or acute infections

Flutter was formerly considered to be due to a circus movement of a stimulus along a regular course most often encircling the entry of the great veins into the auricles stimulating the A V node at regular intervals It is now believed to have the same origin as paroxysmal tachycardia that is the stimuli arise in an ectopic focus in the auricle whose rate is higher than that in paroxysmal tachycardia It forms a distinct clinical entity however and is described separately

Clinical Picture When the pulse remains absolutely regular unaffected by breathing or effort at 80 or 160/min flutter should be suspected There are usually no symptoms unless failure is precipitated by the flutter Vagal stimulation such as carotid sinus compression may suddenly halve the heart rate Effort may double it, if the heart rate is below 100/min In the neck rapid regular pulsations may be seen in the jugular veins In paroxysmal tachycardia carotid sinus stimulation has no effect or it may terminate the attack in sinus tachycardia the rate slowly falls and slowly rises again It has no effect in auricular fibrillation

Prognosis This depends on the state of the myocardium and the cause of the attacks As a rule these are short lived and paroxysmal with sudden onset On occasions however they may last for days weeks or rarely for years If the degree of heart block maintains a normal heart rate the patient remains quite comfortable

Treatment. Digitalis is given in large doses this increases the rate of stimulus formation and converts the flutter into fibrillation On withdrawing the digitalis rhythm often reverts to normal If no digitalis has been given recently 0 6 g (9 gr) of the powdered leaf is given, followed in 6 hr by 0 4 g (6 gr) and in a further 6 hr by 130 mg (2 gr) 130 mg (2 gr) are then given t d s until fibrillation occurs or digitalis intoxication makes one cease treatment

If this is unsuccessful quinidine may be tried This depresses the rate of the ectopic focus and may produce normal rhythm It should never be given without first digitalizing the patient, since

force and volume Thus the beat may vary from one just able to open the aortic valves with a poor second sound and too feeble to reach the wrist to one that is almost normal

Aetiology They may occur in normal individuals and more frequently in the young than in older people Excitement stress alcohol and tobacco increase their frequency They are found with inflammatory and ischaemic conditions *e g* rheumatic carditis or pneumonia and in coronary thrombosis They occur in people who suffer from paroxysmal auricular tachycardia and in mitral stenosis as a precursor to auricular fibrillation They are less common than ventricular ectopic beats

Clinical Picture The majority of patients do not appreciate that an ectopic beat has occurred Some feel a growing emptiness in the chest which may be alarming followed by a thump as if the heart turns over When frequent they may cause troublesome palpitations and induce a fear of serious heart disease

Diagnosis In most cases the premature beat is followed by a pause the succeeding beat being much stronger With auricular extra systoles the abnormal P wave differs in direction and shape and occurs before the next sino auricular impulse The P R interval may be prolonged due to the longer course over the auricles but the QRS T complex is normal in shape The abnormal impulse passes to the sino auricular node causing its premature discharge The sino auricular node then beats at its own rhythm to induce the following heart beat The time interval between the abnormal beat and the next normal beat is therefore the sum of the time taken for the abnormal impulse to travel from the ectopic focus to the sino auricular node plus the normal interval between two beats The condition may be mistaken for partial heart block or if the premature beats follow every other beat complete heart block If they are frequent and irregular they may simulate auricular fibrillation Auscultation is of great assistance in differentiating these

Prognosis They are of no significance clinically Usually the heart is quite normal and if they occur in association with any pathological condition they do not in any way affect the prognosis of the disease process

Treatment If found on routine examination they should be ignored If the patient is aware of them he should be reassured completely that they are of no significance Potassium bromide 0 3 g (5 gr) t d s or other sedative and quinidine 0 3 g (5 gr) t d s may be tried Intake of tea and coffee and the use of alcohol and tobacco should be reduced

Paroxysmal Auricular Tachycardia

This is a rapid beating of the heart of sudden onset the stimulus arising in the auricular musculature It consists of rapidly repeated auricular extra systoles arising as a rule from a single ectopic focus

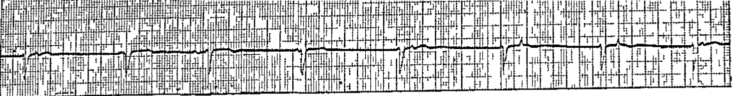
Aetiology It is usually encountered in healthy young adults and does not indicate the presence of any underlying heart disease It may also be found, however in the presence of acute or chronic rheumatic heart disease cardiac infarction or the Wolff Parkinson White syndrome Anxiety stress tobacco or alcohol may seem to be the precipitating cause but as a rule they occur for no apparent reason

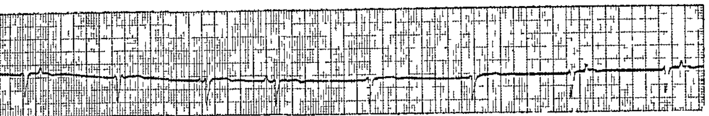
Clinical Picture The symptoms depend on the length of the attack the heart rate and the state of the heart muscle Attacks vary in length from a few beats to those that continue for several days they usually last for a few hours before ceasing spontaneously In the very short attacks a transient fluttering sensation in the chest may be noticed If they continue longer throbbing in the neck veins palpitations with sternal oppression and a sense of anxiety occur A healthy myocardium is able to sustain the tachycardia indefinitely but if coronary artery disease or other abnormality is present, angina or progressive heart failure may develop If the heart rate is very rapid the cardiac output falls and faintness nausea vomiting or actual syncope may occur

The onset is always abrupt An occasional extra systole may precede the attack The blood pressure falls and the pulse pressure is very small The pulse itself is often almost imperceptible The offset may be equally sudden but occasionally no definite ending is noticed The rate may be between 100 and 300/min usually between 150 and 200/min It is quite regular and does not vary with exercise emotion posture or drugs except to be brought suddenly to an end Any heart failure induced by the attack then rapidly improves Death is rare in an attack and only occurs in the presence of severe heart disease

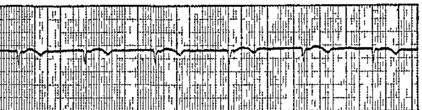
Diagnosis The diagnosis is made most frequently on the history The age of the patient the absence of heart disease despite a long history of such attacks the sudden onset and offset and the measures that customarily produce relief are important points in diagnosis When seen in an attack the heart rate and regularity the absence of distress (unless concomitant heart disease is present) and the sudden cessation when treatment is successful help in diagnosis

It may be distinguished from sinus tachycardia





(a)





(b)

FIG 15 13 WANDERING PACEMAKER AND NODAL RHYTHM

(a) Wandering pacemaker The P wave varies in position in relation to the Q R S complex from beat to beat due to the alteration of the site of impulse formation in the A V node

(b) Nodal rhythm with bradycardia and a period of cardiac arrest

aVF

(a) (b) (c) (d) (e) (f) (g)

Fig 15 11 Auricular Flutter

(a) Flutter at 260 per minute all beats being received by the ventricles
(b) 2 1 block
(c) Irregular block
(d) Sinus rhythm
(e) 2 1 block
(f) Now fibrillating
(g) Sinus rhythm

alone it may so reduce the auricular rate that the A V node responds to all the stimuli the ventricular rate rises to 200/min and serious failure follows if the myocardium cannot maintain this rate

If digitalis and quinidine are unsuccessful in restoring normal rhythm the patient is kept on a maintenance dose of digitalis so that the ventricular rate is kept below 100/min

Auricular Fibrillation (Fig 15 12)

This occurs very frequently and striking clinical improvement may occur when it is adequately controlled It consists of rapid ineffectual fibrillary contractions following each other across the auricles the chambers never being emptied by a concerted contraction With rates of below 380/min this emptying seems possible but above this rate (380–600/min) an effective contraction of the auricle with emptying does not occur The stimuli seem to arise in ectopic foci in the auricular muscle

As in flutter the mechanism used to be considered a circus movement but along an irregular course the A V node being stimulated irregularly as a consequence The ventricular contractions are therefore quite irregular in time and force and usually very rapid

Aetiology This is similar to that of flutter but occurs much more frequently It is characteristically associated with mitral stenosis but is commonly found in older patients with coronary artery disease It frequently occurs with thyrotoxicosis in middle and late life It may occur in paroxysms

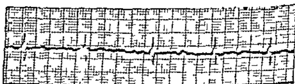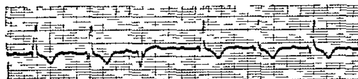
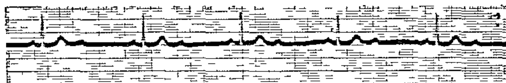


Fig 15 12 Auricular Fibrillation (Lead 2)

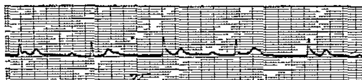


(a)









(b)

FIG 15 14 HEART BLOCK

(a) Sino-auricular heart block. Complete absence of P wave and a consequent dropped beat
(b) Auriculo-ventricular heart block Latent heart block P–R interval prolonged
2 1 block.
3 1 block
Complete heart block.

before becoming permanent Especially in the elderly when myocardial degeneration is present it is easily induced by infection and rhythm may revert to normal on recovery Intoxication e g alcohol smoking food poisoning and even surgical operations may induce it It may be found in other wise normal people and this lone fibrillation may run in families

Clinical Picture *Paroxysmal auricular fibrillation* produces symptoms similar to those of paroxysmal tachycardia When the rate is very rapid praecordial discomfort or angina or even syncope may be produced if the underlying cardiac disease is severe Heart failure then rapidly develops The pulse is completely irregular in time and force the volume depending on the length of the preceding diastolic pause and a marked pulse deficit is present

When established it may produce no symptoms of itself those due to the underlying cause being more evident Heart failure may gradually develop This may be associated with the formation of thrombi in the auricles and dislodgement of these produces arterial emboli of varying size in the brain limbs kidneys etc

In mitral stenosis the presystolic murmur is pro *duced by the passage of blood through the mitral* valve during a normal auricular contraction This does not occur in fibrillation the presystolic mur mur disappears and is replaced by an early diastolic diminuendo murmur its commencement corres ponding in time with the third heart sound

Differential Diagnosis In sinus arrhythmia the irregularity is related to respiration With multiple extra systoles increasing the heart rate results in a more regular rhythm whereas in fibrillation it be comes more irregular, and a pulse deficit may be produced if not previously present Extrasystoles are not common with rates above 100/min Inspec tion of venous pulsation in the neck reveals a complete absence of A waves in auricular fibrilla tion In partial heart block the majority of beats are quite regular this also applies in flutter with irregu lar rhythm The electrocardiogram is essential for exact diagnosis

Treatment In cases of failure rapid digitalization is necessary Digoxin is used 1 0 mg being given followed by 0 5 mg in 6 hr and 0 5 or 0 25 mg in a further 6 hr depending on the heart rate and *provided no* digitalis has been used in the previous three weeks Future dosage depends on the rate of the heart it being kept at about 70–80/min usually 0 25 mg twice or three times a day suffices Digita lization may be produced more slowly in the absence of failure by giving tab dig fol 130 mg *(2 gr) t d s* for 4 days followed by 65 mg (1 gr) t d s or b d as the rate is controlled In certain cases especially in infection rhythm may return to normal on recovery from the infection but this *may not happen In such quinidine is used A test* dose of 200 mg (3 gr) is given and 2 hr later 0 4 g (6 gr) are given every 2 hr for six or seven doses unless rhythm has been restored before this The risk of embolism from auricular clots has to be considered but if rhythm is not restored *fresh clots may form Quinidine should never be tried in cases* of mitral stenosis if heart failure has been present or if fibrillation has continued for longer than two years Fibrillation recurs in uncontrolled thyrotoxicosis and the tachycardia is difficult to slow by digitalis Usually normal rhythm is re established spontaneously if euthyroidism is obtained by neo mercazole or by surgery If this does not happen it will be necessary to use quinidine No advantage seems to be gained by the use of anticoagulants *during quinidine treatment for restoration of normal rhythm*

Nodal Rhythm

This may occur in health or when the sino-auricular node is depressed by infection drugs or mechanically Auricles and ventricles b at syn *chronously There are usually no symptoms* but occasionally the patient experiences a throbbing in the neck the blood filling the great veins with auri cular systole as the A V valves are closed by the simultaneous ventricular contraction

The electrocardiogram (Fig 15 13) shows an abnormal P wave immediately preceding *lost in or immediately following the QRS complex* d pend ing on whether the impulse arises in the upper, inter mediate or distal portion of the A V node

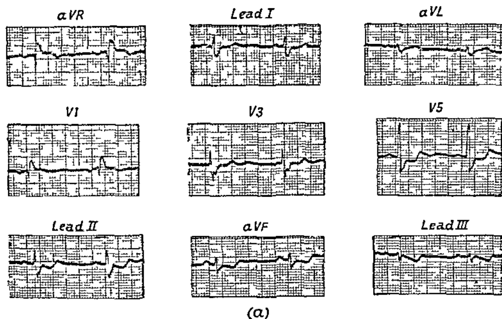
Wandering Pacemaker This condition may be mentioned here the stimulus may arise with suc ceeding beats in the sino auricular node or at varying positions in the auricular ventricular nod It is recognized electro ardiographically by the varying position of the P wave It is associat d with bradycardia and may be induced by digitalis

Auriculo-ventricular Block

This condition indicates interference with conduc tion in the A V node it may be complete or in complete temporary or permanent and it may be caused by structural or functional changes in the node Three grades are recognized—

Grade one latent heart block Conduction *delay* causes the P R interval to exceed 0 2 sec in an adult It is diagnosed by electro cardiography (Fig 15 14) and suggested by a poor first heart sound and a longer pause than usual between the A and C waves in the neck

Grade two incomplete heart block Fatigue *of*



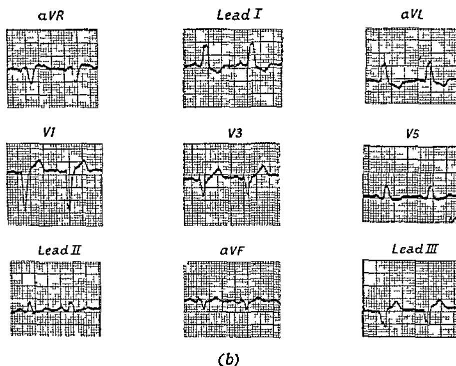


FIG 15 15 RIGHT AND LEFT BUNDLE BRANCH BLOCK

(*a*) Right
(*b*) Left

the A V node causes increasing delay with lengthening of the P R interval until no conduction occurs and a beat is missed the Wenckebach phenomenon Recovery of the node occurs and the cycle is repeated Alternatively the prolonged P R interval remains constant and every second third or fourth beat is dropped 2 1 3 1, or 4 1 block Regular dropped beats are recognized at the wrist they are distinguished from extrasystoles by the absence of the premature preceding beat and the absence of a ventricular contraction on auscultation at the apex *An auricular wave is seen in the neck* without a consequent first sound at the apex

Grade three complete heart block In this condition none of the impulses is conducted to the ventricles which beat at their own intrinsic rhythm Usually this is 30–40/min and the rhythm is regular The auricles beat at 70 or so per minute their rate being affected normally by exercise emotion or drugs but the ventricles continue to beat at their intrinsic rate Auricular A waves may be seen synchronous with those in the neck The relationship *between the auricular and ventricular contractions* may be very variable so that the loudness of the first sound may also vary when the auricles and ventricles contract simultaneously large A waves may be seen in the neck

Aetiology The commonest cause is ischaemic heart disease any grade of block results and it is usually progressive and permanent Arteriosclerotic rheumatic or syphilitic fibrosis or calcification of the aortic valve may spread locally to involve the A V node or Bundle of His to produce similar results Aschoff nodes syphilitic gummata neoplasms or haemorrhage may compress or invade the conducting tissues Congenital lesions may produce heart block and may be discovered at any age this *is most often associated with interventricular septal* defects In the past diphtheritic infections commonly caused severe degrees of heart block Rheumatic fever frequently produces latent heart block and less often more severe grades This is partly due to vagal effect and is removed by atropine Vagal stimulation as by carotid sinus compression may induce any degree of heart block Digitalis may also produce heart block partly by vagal effect partly by its direct depressant effect on the conducting tissue

Clinical Picture There are no symptoms of latent heart block. Second degree block occasionally causes palpitations due to the consciousness of the dropped beat Complete block usually causes no symptoms but if the rate is very slow faintness is experienced When the rate drops below 8/min or if the ventricle either ceases to contract or fibrillates Stokes Adams attacks occur

Stokes Adams Attack The heart may cease to beat when partial block becomes complete or less commonly when the idio ventricular rhythm becomes depressed Asystole causes immediate cessation of the circulation and unconsciousness results in a few seconds suddenly and without warning due to cerebral anoxia The patient is pale and *pulseless heart sounds cannot be heard and a blood* pressure cannot be recorded If asystole continues for 15 sec or more convulsions occur and if recovery does not take place in two minutes death usually results Slight attacks may be quite short with fleeting loss of consciousness or slight faintness They may occur at any moment at rest or when active They vary in frequency in some cases occurring every few months but in severe cases they succeed each other every few hours or minutes even while at rest in bed On recovery the oxygenated blood from the lungs floods the dilated capillaries and arteries a rich pink colour spreading over the body which quickly fades Prognosis is poor when these occur frequently death occurring *in such an attack due to prolonged* asystole or ventricular fibrillation

Treatment As auriculo ventricular block usually gives rise to no symptoms treatment for it is rarely needed though treatment may be required for the underlying cause (such as ischaemic heart diseas syphilis or digitalis over dosage) Stokes Adams attacks can occasionally be prevented by ephedrine 30 mg (½ gr) t d s or isoprenaline 15 mg under the tongue t d s which increase the sympathetic tone Vagal influence may be diminished at the same time by atropine 0 5–1 mg (1/100–1/50 gr) t d s Thyroid may be given a cautious trial it may induce heart failure in advanced cases Barium salts are not helpful If attacks are very frequent 1 ml adrenaline in *oil is given intramuscularly for its prolonged* effect.

In the attack itself recovery occurs often before any active steps can be taken to cut it short If asystole continues however adrenaline 0 5 ml is given directly *into the left ventricle* Ideally an electrocardiogram should be taken to exclude ventricular fibrillation as adrenaline then only increases the danger Quinidine and procaine amide are contra indicated In the presence of heart failure digitalis is given in the usual way

Bundle Branch Block (Fig 15 15)

This is said to be present when *conduction in one* or other of the bundle branches is affected Lesions usually exist in both divisions but one side is more involved than the other

Aetiology Pathological lesions *mainly affecting* the left ventricle are ischaemic heart disease hyper tension and aortic valve lesions these result in left

syndrome one ventricle is stimulated from the auricle by an abnormal path of conduction and the result *simulates a bundle branch block*

Clinical Picture The symptoms are those of the underlying disease There are often no signs but the condition must be considered when the first sound at the apex is reduplicated and the pulmonary second sound split. A double impulse may be felt at the apex with systole Electrocardiographically the QRS complex is lengthened to 0 1 sec and usually to 0 12 sec or longer In left bundle branch block the left ventricle is stimulated by spread from the right ventricle Muscle conduction is slower the electrical changes over the left ventricle occur later accounting for the prolonged QRS complex Chest leads give a clearer indication of the bundle at fault

Prognosis Bundle branch block may be innocent and apparently make no difference to prognosis It may be transient especially when due to temporary toxic states The condition however is usually associated with severe pathological changes in the ventricular myocardium The outlook depends on the cause of these changes and its response to treatment A large number of patients die within 2-3 years after it has been discovered

Treatment. There is no treatment except for the underlying condition Quinidine and procaine amide hydrochloride should be avoided

Ventricular Rhythms

Ventricular Escape

When the ventricles fail to be stimulated from the A V node for any length of time impulses arise in a lower focus usually in the Bundle of His before its bifurcation so that the QRS complexes are of usual contour The rate is 30–40/min

Ventricular Premature Contractions (Ventricular Extrasystoles)

These closely simulate auricular extrasystoles and can be distinguished only by electrocardiography (*see* Fig 15 17) They tend to occur in older patients than auricular premature contractions They may occur in healthy people or in those with ischaemic or hypertensive heart disease or heart disease associated with infection or infarction With heart failure they become less frequent as improvement occurs Anxiety excessive smoking tea coffee and digitalis also produce them

The symptoms are similar to those of auricular extrasystoles Electrocardiographically it is seen

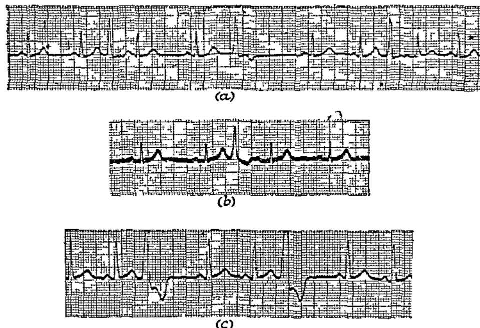


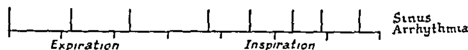
FIG 15 17 VENTRICULAR EXTRASYSTOLES

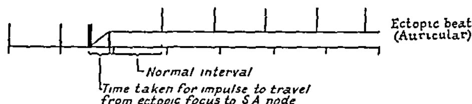
(*a*) An interpolated ventricular extrasystole and a dropped beat
(*b*) An interpolated extrasystole
(*c*) Dropped beats

bundle branch block Pulmonary hypertension due to mitral stenosis pulmonary infarction inter auricular septal defects or emphysema result is right bundle branch block Infection may cause either as may digitalis quinidine or pronestyl and toxic states such as uraemia and thyrotoxicosis It may be present with myocardial infarction

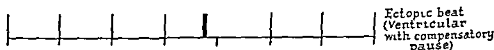
Congenital right bundle branch block is not rare and may be found in the presence of a normally functioning heart In the Wolff Parkinson White













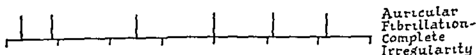


Fig 15 16 Illustrating Various Rhythms

Sinus rhythm is usually quite regular and this regularity is marked on the succeeding types of rhythm below the base line In auricular ectopic beats the sino-auricular node rhythm is interfered with and a new rhythmicity started This is indicated by a raised base line the lower base line indicating where the original sinus beats would have occurred

syndrome one ventricle is stimulated from the auricle by an abnormal path of conduction and the result simulates a bundle branch block

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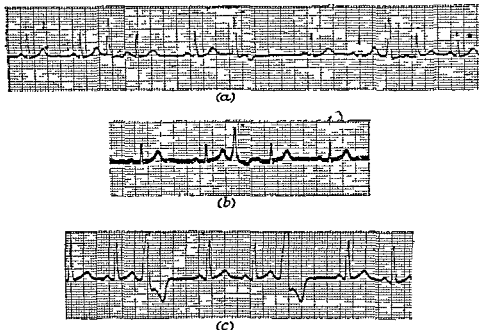


FIG 15 17 VENTRICULAR EXTRASYSTOLES

(*a*) An interpolated ventricular extrasystole and a dropped beat
(*b*) An interpolated extrasystole
(*c*) Dropped beats

that a compensatory pause follows a premature contraction so that the sum of any two cycles is equal The beat arises *from an irritable focus in one or* other ventricle and the outline of the QRS complex shows in which ventricle the beat originated It is similar to that seen in bundle branch block

Treatment This is similar to that for auricular premature contractions In the great majority of cases their presence goes unnoticed by the patient and they should be ignored Should they cause symptoms by their force and frequency and give rise to anxiety the following measures may be tried If they are due to digitalis the dose is reduced Procaine amide hydrochloride (Pronestyl) 0 25–0 5 g t d s is very effective or quinidine 0 4 g (6 gr) t d s may be tried Potassium salts also diminish their formation Sedatives may help sometimes and the patient is reassured strongly that any symptom he may feel due to the ectopic beat is not indicative of *the possibility of severe heart attacks*

Ventricular Tachycardia

This is much less common than auricular tachycardia is usually associated with serious heart disease occurs in older patients and has a correspondingly more serious prognosis In a few cases there is no underlying disease It may last a few beats only or several hours or days In the latter case the fall in output and drop in blood pressure combined with myocardial damage leads to gradual heart failure or sudden death from ventricular fibrillation The symptoms are similar to those of auricular tachycardia If the auricles are beating regularly variation in the time of contraction of auricles and ventricles causes variation in the intensity of the first sound and the A waves in the neck The diag*nosis is made by electrocardiography (Fig 15 18)*

Treatment Procaine amide hydrochloride (Pronestyl) is the drug of choice If the condition of the *patient is grave it is given slowly* intravenously 1 g is dissolved in 50 ml of water the injection being given not faster than 5 ml/min Not more than 1 g is given at a time and the blood pressure *is taken continuously the injection being stopped* if a severe fall in blood pressure occurs An electrocardiogram is taken simultaneously When regular rhythm is restored the injection is stopped and the drug continued by mouth 0 25–0 5 g eight hourly In less urgent cases it may be given by mouth. Quinidine is often effective in doses similar to those used in auricular fibrillation It may be given with great care intravenously Digitalis is avoided because of its irritant action on the ventricles it may induce ventricular fibrillation If heart failure supervenes however it should be used Other methods employed are 20 ml of 20 per cent magnesium sul*phate intravenously, or morphine sulphate 15 m* (¼ gr) intravenously

Ventricular Fibrillation

The ventricular muscle contracts in a completely uncoordinated manner so that it fails to expel its contents and unconsciousness and death rapidly follow Short attacks may cease spontaneously It is produced by anoxia as when excessive demands are made in ischaemic heart disease or aortic valve affections Adrenaline digitalis or chloroform may produce it and it may occur in infarction and at the end of a Stokes Adams attack producing death Quinidine or procaine amide hydrochloride may be injected into the heart and these drugs should be given prophylactically under conditions that may produce fibrillation of the ventricle

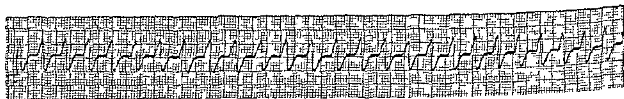
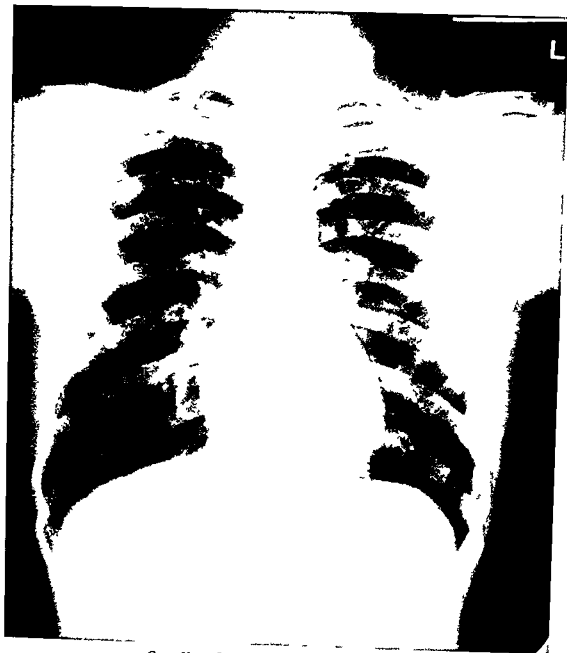


FIG 15 18 VENTRICULAR TACHYCARDIA

HEART FAILURE

The heart and blood vessels form a closed system whose function is to maintain an adequate supply of blood to all the tissues of the body including the heart and vessels themselves The force is supplied by the contractions of the myocardium which *acts on the blood returned* to the heart pumping it out against a variable resistance Changes in each of these factors influence the cardiac output When *output falls below the level necessary for* adequate nutrition of the tissues heart failure is present This implies that the compensatory mechanisms to be described have occurred but the cardiac reserve has decreased beyond the point of adequate cardiac output at rest



Chest X ray Showing a Normal Heart Outline



Hypertensive Heart Disease Showing Moderate Hypertrophy of the Left Ventricle

Cardiac Reserve

The needs of the body vary from moment to moment as in exercise emotion pregnancy or fever The ability of the heart to increase its work to meet these variable needs is known as the cardiac reserve It can be increased in health by training and is steadily diminished in cardiovascular disease It is the algebraical total of a number of compensatory *mechanisms which come into operation* and are—

1 Tachycardia, 2 Dilatation, 3 Hypertrophy — Cardiac
4 Increased blood volume, 5 Redistribution of blood — Extra cardiac

Each of these mechanisms is self limiting in that beyond a certain point cardiac output no longer increases but falls as the compensatory mechanism increases and so leads to increasing failure

Tachycardia This is an inefficient method of in*creasing cardiac output and is soon replaced by a* greater stroke output that is by dilatation especially when it occurs as an immediate response to sudden effort It is also seen in the terminal stages of heart failure when it indicates a serious prognosis When the diastole is so shortened that the rapid filling stage of the ventricular cycle is diminished output falls

Dilatation Whenever ventricular emptying in systole is incomplete dilatation occurs The ventricle enlarges to contain the venous return during diastole as well as the retained blood from the previous systole This leads to a more powerful contraction and greater output Beyond an optimum point however increased ventricular dilatation causes a weaker beat and failure occurs

Hypertrophy The cause is unknown each myocardial fibre increases in size but the number of capillary vessels supplying these fibres remains unchanged Compared with the increase in myocardial fibre volume the surface area increase through which metabolic exchange occurs takes place at a relatively decreasing rate (the square as compared with the cube of the radius) Oxygen diffusion into the cell also takes longer (as the square of the distance of the diffusion) and these three facts limit the advantage to be gained by a continued increase of muscle volume In many cases hypertrophy is associated with coronary artery disease which tends to reduce the available oxygen and further diminishes the value of increasing muscle volume As in dilatation there is an optimum level of hypertrophy beyond which no advantage is obtained

These mechanisms are present for a considerable time before clinical failure occurs but there is always an accompanying diminution in cardiac reserve The degree of dilatation and hypertrophy is a measure of the reduction in cardiac reserve The need for tachycardia on increased effort is a basis of the exercise tolerance test.

Increased Blood Volume This occurs whenever systemic venous pressure is increased There is an alteration in the secretion and re absorption of sodium and chlorine by the kidneys with retention of salt and water The mechanism is not completely understood it does not seem related to rise in venous pressure in the kidneys suprarenals or pituitary gland but in the systemic and pulmonary venous system generally A similar result is seen after giving D O C.A and increased amounts of this hormone have been found in patients in heart failure The effect may be added to by the lowered cardiac output and diminished circulation rate the effect on the kidney blood flow being much more marked than that in other organs This is by no *means proved as even large changes in glomerular* filtration rate can be compensated for by minute changes in tubular re absorption rate The increased blood volume raises the venous pressure and the filling pressure of the chambers of the heart with consequent increased force of contraction and increased cardiac output. Beyond a critical level however this mechanism also fails as the heart muscle is over distended with consequent diminution of output The rise in venous pressure continues however and oedema results

Redistribution of Arterial Blood Whenever the cardiac output falls either rapidly as in shock or peripheral circulatory failure or gradually as in progressive heart failure so that the blood supply to the vital organs is imperilled this reaction occurs The arterioles and capillaries in the skin splanchnic area and muscles contract due to nervous and hormonal reflexes diverting the blood to the heart lungs and brain This is the cause of the cold grey skin of patients in such extremity In chronic heart failure it is seen with the tachycardia rapidly dilating heart and falling blood pressure of the dying patient

High and Low Output Failure

These terms have been introduced following work on measurements of cardiac output As the heart fails its output falls but certain cases of failure were found whose output was much higher than some cases not in failure It was shown that failure in such cases was due to extra cardiac causes—a large shunt as in arteriovenous aneurysm or Paget s disease inadequate oxygenation as in emphysema or anaemia inadequate nutrition as in beri beri or an increased metabolic need as in thyrotoxicosis In

these cases the cardiac output is raised and even though failure has occurred it remains higher than normal When the cause is primarily cardiac the output is low Examples of both causes operating simultaneously can be multiplied Emphysema and hypertension often occur together as do anaemia and bacterial endocarditis

Forward and Backward Failure

In heart failure congestion occurs in the chambers and venous system behind the failing heart chamber and the output falls One school of thought explains all the signs and symptoms of failure by diminished output the other by the resultant congestion but neither theory explains all the aspects of heart failure Both facts are correct and are linked by the failure of the compensatory mechanisms

Causes of Failure

We can recognize heart failure but the reason for failure at any moment is still unknown There is no characteristic pathology at post mortem or histologically The changes seem to be intracellular in the essential metabolic processes of the muscle fibres The three factors already mentioned myocardial contraction venous return and resistance to blood flow, may contribute the main cause Myocardial contraction is impaired by infection or inadequate nutrition the latter being possibly due to coronary artery disease anaemia avitaminosis a low blood pressure or tachycardia Resistance to blood flow is seen in hypertension or valvular stenosis The venous return may be inadequate as in shock peripheral circulatory failure or venous thrombosis either systemic or pulmonary In high output failure the myocardium is incapable of sustaining the rapid circulation and fails

Left sided Heart Failure

The work of the left and right sides of the heart differs considerably and conditions in the lesser or the greater circuit may cause failure of one side independently of the other

Aetiology Left ventricular failure may be caused by hypertension coronary artery disease or lesions of the aortic valve Mitral regurgitation may also cause left ventricular failure mitral stenosis however results in failure of the left auricle

Mechanism The left side of the heart receives blood from the right ventricle but in left sided heart failure is unable to cope with it. A rise in pressure in the pulmonary circuit with engorgement of its vessels results The dilated vessels encroach upon the residual air the rise in pulmonary circuit pressure diminishes the elasticity of the lungs both factors reducing the vital capacity Nervous reflexes from the great veins and alveoli increase the rate of respiration and this together with the diminished elasticity and vital capacity causes marked dyspnoea

Orthopnoea is usually present at this stage the patient breathing more comfortably when sitting up The horizontal position increases the venous return and blood is pumped into the pulmonary vessels at a faster rate In left ventricular failure this adds to the pulmonary engorgement The horizontal position also raises the diaphragm so diminishing the thoracic volume and increasing the work of respiration These factors increase the respiratory distress in the horizontal position which is relieved by sitting upright

The rise in pulmonary pressure also raises the pulmonary capillary pressure causing a greater transudation of fluid into the interstitial tissues of the lung At first this is removed by the lymphatics but as it increases fluid passes through the basement membrane with the expectoration of clear frothy phlegm Pleural effusions develop more frequently on the left side in left ventricular hypertrophy and on the right in mitral stenosis These may develop quietly and insidiously and decrease still further the vital capacity The right ventricle eventually fails with general venous engorgement. The blood flow to the lungs is diminished and the pressure in the lesser circuit correspondingly reduced The patient s dyspnoea is markedly diminished and he feels much more comfortable although at this point failure is more severe and prognosis worse

Paroxysmal attacks of dyspnoea may occur which may progress to acute pulmonary oedema These conditions develop whenever there is a sudden deterioration in (1) the efficiency of the left heart or (2) a sudden increase in its load It is seen therefore in coronary thrombosis which diminishes the strength of the left ventricle The load increases when the venous return rises when the blood pressure is raised or in tachycardia Tachycardia is especially important in mitral stenosis as it diminishes the time available for the blood to pass through the narrowed mitral valve Nocturnal attacks of paroxysmal dyspnoea are characteristic of left ventricular failure During sleep the general metabolism is lowered and the impaired circulation is more capable of dealing with it interstitial oedema is absorbed the blood volume is raised and the venous return increased This is added to if the patient slumps during sleep into a more horizontal position Sudden movements of large muscles during sleep compress the dilated capillaries and large veins between the muscle masses with sharp increase in venous return The rise in pulmonary

capillary pressure may reach higher levels than normal before the usual reflexes occur When eventually the laboured breathing awakens the patient dyspnoea is marked he experiences intense distress and in severe cases frightening suffocation He fights for breath and struggles into a sitting position his efforts increase the venous return his fear increases the secretion of adrenaline a rise in blood pressure and pulse rate result and this increases the load of the left ventricle A critical level is reached when the pulmonary capillary pressure equals the osmotic pressure of the blood Pulmonary oedema is increased and frothy fluid may pour into the alveoli when extreme the fluid is pink with red cells carried through by diapedesis Right heart failure and general venous engorgement often occurs at this stage with cyanosis due to impaired aeration of blood The cyanosis is due to the flooded alveoli and thickened oedematous basement membrane

Clinical Picture The earliest symptom is increasing dyspnoea on effort and the best assessment of this is a careful history from the patient himself Provided increasing obesity lung disease or general disease such as anaemia can be excluded increasing dyspnoea on effort is a measure of the increasing congestion of the pulmonary circulation and of the diminishing reserve of the left heart The patient himself first notices the slightly deeper and more rapid breathing necessary for tasks he could previously do in comfort As the condition advances it becomes evident also to the onlooker There is also an unaccustomed lassitude and weakness Dyspnoea becomes increasingly more easily induced until it is present at rest Orthopnoea develops and the patient gains most ease sitting upright with the legs hanging down Cough on effort develops as when undressing to retire at night or it may waken the patient in the small hours It is dry and irritating or there may be a small amount of clear phlegm Later attacks of paroxysmal nocturnal dyspnoea occur infrequent at first and perhaps lasting only a few minutes receding as the patient sits up They became more frequent and prolonged and the patient comes to dread them He wakens at about two or three a m gasping for breath with a sense of suffocation and occasionally oppression or actual pain of an anginal type over the chest He sits up gasping and frightened He may walk about and attempt to open the windows hoping thus to gain relief He is bathed in perspiration with dilated pupils and pale skin but the jugular venous pressure is not raised unless right ventricular failure has also occurred The blood pressure rises and the pulse rate increases characteristic findings in paroxysmal nocturnal dyspnoea The respirations are laboured and rapid and as the pulmonary oedema increases becomes wheezy with moist sounds audible at a distance In acute pulmonary o dema the fluid in the large tubes causes loud gurglings and frothy fluid in abundance may pour from the mouth and nose This may be pinkish or blood stained The patient may become increasingly cyanosed and if right failure develops the jugular venous pressure becomes raised and the liver engorged If the condition is irreversible failure advances and peripheral circulatory failure results he becomes grey and ashen with falling blood pressure but a very rapid pulse and dies Usually recovery occurs and all these changes regress the patient becomes calmer and more restful the blood pressure falls to its normal level and the lungs clear Prognosis however is poor and the patient may gradually enter progressive heart failure Life does not continue as a rule for more than two years after the attacks begin and he may develop at any time ventricular fibrillation Paroxysmal dyspnoea is most commonly due to hypertension less frequently to coronary artery disease and aortic valve disease In mitral stenosis it is frequently due to tachycardia of any sudden emotion or effort and in pregnancy due to the associated increased blood volume it is much more easily induced

Cheyne Stokes respiration is frequently found in left ventricular failure it is a periodic waxing and waning of respiration each cycle taking about a minute It occurs in conditions which diminish the sensitivity of the respiratory centre and so is met with during sleep in the elderly and arteriosclerotic after head injuries in uraemia or following the taking of sedatives In left ventricular failure it is also found in sleep or after sedation and is caused by the combination of depression of the respiratory centre and reflex hyperventilation due to the pulmonary congestion The increased ventilation washes out excessive amounts of carbon dioxide The depressed respiratory centre fails to respond promptly to this lack The consequent apnoea is prolonged also and an oxygen lack is built up This sensitizes the respiratory centre to the re accumulating carbon dioxide and over ventilation again follows These phases of apnoea and hyperpnoea increase in intensity and the hyperventilation may be so violent as to waken the patient and cause continuous interference with sleep It is relieved by the administration of oxygen or of carbon dioxide

When the left ventricle fails the heart is always enlarged the apex beat being displaced downwards and outwards Hypertension or aortic valve disease may also be pres nt It has a slow lifting or heaving character This quality of apex beat may be found

with a normal or low blood pressure and then indicates extensive myocardial damage If mitral stenosis is the cause of the left heart failure the usual signs of this condition are present In left ventricular failure a triple rhythm is present at the apex When tachycardia is also present the sounds have the quality of a gallop rhythm When loud it is accompanied by an extra impulse over the left ventricle

The pulmonary second sound is accentuated and split and may exceed the aortic second sound in intensity It is a measure of the rise in pulmonary pressure and is very evident in mitral stenosis the second or pulmonary element being notably increased As failure progresses the heart sounds become more muffled In the lungs air entry may be poor at the bases crepitations may be heard or an effusion found Alternation of the pulse is of serious import its cause is not understood Strong and weak contractions of the ventricles alternate with alternation in the blood pressure of from 1 or 2 mm of mercury to 20 mm or more The rhythm is regular and this condition should not be confused with pulsus bigeminus this is caused by regular extra systoles the weaker beat being nearer the preceding strong beat Slight degrees of alternation can be appreciated only by the sphygmomanometer more severe conditions can be recognized by feeling the pulse

As the condition advances radiologically the heart is seen to be enlarged due mainly to enlargement of the left ventricle The pulmonary vessels become engorged and when oedema develops patchy mottling appears first at the hila spreading outwards as the condition progresses Effusions may be seen at the bases quite unsuspected when small They occur at either side more frequently on the left in hypertensive failure and on the right in mitral stenosis

The circulation time is measured by injecting substances having a distinctive taste easily recognized by the patient Three to five ml of a 20 per cent solution of sodium dehydrocholate is injected rapidly into the ante cubital vein the patient signalling as soon as he tastes it in the mouth Saccharin or calcium gluconate solutions may be used Radioactive sodium has been employed the passage of the metal through the circulation being plotted by a Geiger Muller counter In left ventricular failure the time is prolonged from the normal 9–18 sec to 25 sec or over the delay being due to the slow passage of blood through the engorged pulmonary veins This test is almost never used The vital capacity is greatly diminished The basal metabolic rate is raised in failure probably due to the enlarged heart and the increased work of the respiratory muscles These investigations are mentioned as being of interest but they are seldom used in practice

In acute pulmonary oedema the patient is pale and sweating profusely the pulse is raised and the blood pressure high The air entry is diminished and as the condition advances fine crepitations develop over the lung bases spreading upwards to include the whole lung fields anteriorly and posteriorly They become coarser in character as the fluid increases in amount and moves into the larger bronchi until loud gurglings may be heard at a distance from the patient Blood stained fluid may be expectorated and as it increases in quantity it may pour from the mouth and nose

Differential Diagnosis Increasing dyspnoea on effort may be due to anxiety obesity or lung conditions such as emphysema asthma or bronchial carcinoma Anaemia and debility following acute infections also increase dyspnoea on effort. The onset of paroxysmal dyspnoea due to left ventricular failure in its early stages is almost indistinguishable from bronchial asthma but a careful history will help to distinguish them In left ventricular failure crepitations are found at the bases and watery frothy fluid may be produced these findings not being present in an asthmatic attack The circulation time is normal in asthma prolonged in left ventricular failure

Treatment This is the same as for right heart failure and will be discussed later Acute attacks of paroxysmal dyspnoea however and especially if these progress to pulmonary oedema have to be treated as medical emergencies The patient is propped well up in bed and the legs allowed to hang down thereby diminishing the venous return Morphia is given 15–20 mg (¼–⅓ g) to allay restlessness and anxiety also to depress the respiratory centre Aminophylline 0·4 g is given intravenously if bronchospasm is present and whenever doubt exists about the cause of the spasm when adrenalin is avoided If due to hypertension dramatic relief is gained by intravenous hexamethonium compounds (30 mg) Digitalis should be given if these methods fail It may strengthen the right heart more rapidly than the left so increasing the pulmonary congestion at first until the left heart also improves in practice however it is never omitted in severe cases Digoxin 0·5 mg is given intravenously repeated in half an hour if the patient is not improving Oxygen is only of value if cyanosis is present it is given under pressure when it may diminish venous return and pulmonary permeability Mercaptomerine (Thiomerin) or mersalyl relieve pulmonary congestion by excretion of sodium and water They are of little value during attacks but may prevent or diminish their occurrence If the condition pro

gresses despite these measures tourniquets are placed round the thighs to obstruct the veins releasing them alternately for 10 min every ½ hr If the condition is seriously deteriorating venesection is carried out ½–1 pint being allowed to escape rapidly through a large bored needle This should not be carried out if anaemia is present it may well precipitate shock which is irreversible

Right Heart Failure

When the right heart fails the mechanism is the same but now the right ventricular output fails

Aetiology The commonest cause of failure of the right ventricle is progressive left sided heart failure The rise in pulmonary circuit pressure leads to dilatation and hypertrophy of the right ventricle which ultimately fails in its turn This leads to lowering of right ventricular output with diminution in pulmonary congestion and some relief of dyspnoea

Hyperkinetic circulatory states cause an overloading of the heart as a whole and ultimate failure with systemic congestion The same result follows toxic conditions in infections Tachycardias if long sustained and especially with coronary artery disease or associated with other causes of myocardial stress have the same result It occurs too in constrictive pericarditis and in dorsal kyphosis These conditions cause right heart failure as part of a general heart failure and so are better named congestive heart failure The right ventricle itself fails in chronic pulmonary disease especially in emphysema and in congenital lesions with a left to right shunt or pulmonary stenosis

Clinical Picture When the right heart failure is consequent on failure of the left heart dyspnoea may be relieved at first if it follows pulmonary or general cardiac causes dyspnoea is steadily progressive Weakness and fatigue increase The general congestion results in oedema and affects the function of the brain liver and kidneys The oedema at first is latent and as it increases the patient may put on over a stone in weight It manifests itself first towards the end of the day in dependent parts where there is loose connective tissue thus it is seen around the heels and over the dorsum of the feet It disappears during the night as the metabolism decreases and the cardiac output becomes adequate Soon it lasts the whole day increasing still towards evening It extends up the legs to the knees and thighs and later affects the genitals and trunk When the patient is in bed it is first found over the sacrum in the genitals and behind the thighs and ankles It may increase so that striae form and fluid may ooze from the slightest trauma to the skin The skin capillaries are compressed and the skin is cold and pale Eczema and cellulitic areas form When heart failure follows emphysema and orthopnoea is absent oedema of the face may be present in the mornings Oedema is due to retention of sodium and fluid with resulting increase in blood volume its site of original formation in lung or body generally depends on whether the left or right ventricle fails first Once the intracapillary pressure exceeds the osmotic pressure oedema results When the circulation rate is markedly slowed endothelial anoxaemia may add to this tendency and in the presence of hypoproteinaemia it is also increased

Cyanosis does not necessarily indicate congestive heart failure It is a measure of the amount of reduced haemoglobin in the blood and at least 5 0 g/ml must be present before cyanosis can occur Thus in severe anaemia it may be impossible for cyanosis to be seen A slow skin circulation rate as when capillaries are dilated and the arterioles are constricted can produce it when the cardiovascular system is normal Central cyanosis is produced when there is a right to left shunt or when the blood in the lungs is not adequately aerated as in pulmonary oedema or advanced emphysema The tendency to cyanosis is increased in polycythaemia or when the skin capillaries are dilated it is lessened when the capillaries are constricted

Attacks of bronchitis are frequent and increase the failure The toxaemia depresses the myocardium and the infection impairs the efficiency of the lungs Haemoptysis is frequent and infarcts may form usually due to emboli from venous thromboses in the legs Palpitations the consciousness of the heart s action do not themselves indicate cardiac disease They are due to anxiety or a change in rhythm of the heart *e g* extra systoles or paroxysmal tachycardia or increase in output *e g* anaemia exercise or thyrotoxicosis

The urinary output falls as failure advances and oedema increases Nocturia interferes with sleep as reabsorption of interstitial fluid then takes place and the urinary output rises Anorexia flatulence nausea and vomiting are commonly found due probably to venous congestion of the stomach and small bowel A constant aching in the right hypochondrium may be troublesome caused by the liver engorgement and the stretching of its capsule Loss of weight amounting to cachexia occurs in advanced failure This is due to the combination of anorexia small bowel oedema and liver congestion interfering with absorption and metabolism The basal metabolic rate is raised and protein is also lost in exudates and the urine This wasting is obscured by the oedema in the lower limbs but is seen over the shoulders and arms

Cerebral anoxia due to diminished cardiac output

results in lack of concentration forgetfulness and poor sleep, disturbed by vivid dreams Fitful dozing may take place during the day and insomnia by *night These symptoms fluctuate considerably* so that hour by hour the patient may be bright and wakeful, or somnolent and forgetful They are ac centuated by concomitant cerebral arteriosclerosis or thrombosis Less commonly he becomes con fused *quarrelsome paranoid or depressed if there* had previously been any such tendency

Venous thromboses in the legs are common but may be overlooked due to the oedema present Small pulmonary infarcts with pain cough and haemoptysis may follow a large one may cause sudden death Pleural effusions which form may be heavily bloodstained If multiple pulmonary infarcts occur *the patient may become jaundiced This is* increased by the hepatic congestion in prolonged failure cirrhosis may develop

The most important sign of systemic congestion is a rise in the jugular venous pressure At 45° no venous pulsation should be visible above the clavicle As congestion increases however pulsation is seen at increasingly higher levels in the neck *When the top of the pulsating column of blood in* the external jugular vein reaches the ears it may stand out as a solid cord without apparent pulsa tion but the lobe of the ear can be seen to move with systole The root of the neck must be relaxed by bending the head a little and rotating it to the right If in doubt the vein may be emptied from below upwards and kept empty by pressure at the *upper point the vein is seen to fill from below Or* pressure may be applied below when the vein fills on releasing the pressure it is easy to see the upper level of pulsation after the vein has partly emptied

There is usually a tachycardia but the rate may be normal The heart sounds may be little affected but as a rule the first heart sound is quiet If failure is due to valve defects the murmurs may become less loud as the force of contraction decreases The blood pressure is usually raised in failure due to *the increased blood volume When failure is extreme* it falls towards the end as the peripheral vaso constriction fails and death is then very near As improvement takes place *the blood pressure falls* to its usual level In some cases the usual rise does not take place the pressure remaining steady or even falling at an early stage

The liver enlarges the rate depending on the rate of failure If this is rapid considerable pain is felt in the right hypochondrium and when associated with vomiting may cause confusion in diagnosis It may reach the umbilicus in advanced cases It is smooth in outline and soft unless cirrhosis has occurred *Ascites is due to engorgement in the portal* system It is a feature of cardiac cirrhosis causing great discomfort and necessitating repeated tap pings

Hydrothoraces also form more frequently on the *left in left heart failure* and more frequently on *the right in right heart failure* They add greatly to the dyspnoea

The urine is diminished in amount and its specific gravity is raised unless failure is due to hypertension consequent on nephritis The urinary chlorides are low unless diuresis is occurring Albumin is present in considerable amounts and granular casts with white and less commonly red cells may occur The blood urea is raised to 80–100 mg p r cent, even when the kidneys are normal this falls to normal *when failure is relieved*

Serial X rays of the chest show the heart to be enlarging and it may reach an enormous size Movements of the ventricles are poor This in[illegible] in heart size adds to the respiratory embarrassment by diminishing the vital capacity Pleural thickening due to oedema and pleural effusions may also be present

The basal metabolic rate is raised (cf p 248)

Hypoglycaemia may be severe due to liver dysfunction and the increased metabolism

Differential Diagnosis An enlarging liver with ascites and consequent oedema of the legs is met with in cirrhosis and in secondary d posits in the liver with or without peritoneal carcinomatosis The dyspnoea and the oedema of the legs are due to *the increased intra abdominal pressure* raising the diaphragm and compressing the inferior vena cava In congestive heart failure the dyspnoea precedes the oedema in cirrhosis th- *ascites* precedes dyspnoea The nephrotic syndrome also results in general anasarca and dyspnoea with a low urinary output *The cardiovascular system is normal* how ever and the characteristic urinary and blood chemistry findings of nephrosis make the diagnosis clear

Chronic constrictive pericarditis is described on *page 275*

Oedema due to local causes such as varicose veins or pelvic causes *e g* carcinoma of the prostate or *ovarian tumours should not cause difficulty* The cardiovascular system is normal unle s associated with cardiovascular disease a search must be made for the cause of local oedema

Treatment Treatment is aimed at (1) resting the heart and (2) increasing its efficiency Th- only means of resting the heart is by resting the patient mentally and physically *The completeness and dura tion of physical rest depend on the severity of the failure and the response to treatment* In advanced

cases treatment may have to be continued for many weeks for an average case 3-6 weeks are usually necessary while for a mild case responding rapidly to treatment only a few days may suffice Rest in a heart bed with the legs dependent and the back raised is needed for severe cases or the patient may be nursed reclining in a comfortable arm chair This diminishes the venous return and therefore the work of the heart and allows the oedema to collect in the legs It allows better expansion of the lungs and the patient is able to move his ankles and knees so reducing the *likelihood of venous* thromboses and pulmonary infarction and infection A commode is always preferable to a bedpan As orthopnoea disappears and effort tolerance improves he is allowed to move about the bedroom and then from room to room on the same floor Mental rest is obtained by avoiding business worries and associates and on returning to work the patient should start part time delegating as much as possible to others

Adequate sleep should be ensured by the use of hypnotics especially in the early stages Morphine 15–20 mg (¼–⅓ gr) by injection or Nepenthe 1–1 5 ml by mouth is given in decreasing amounts as improvement occurs and barbiturates or other hypnotics are substituted as early as possible During the day sedatives should be given to diminish anxiety and encourage peace of mind Diet is also important in obtaining rest by reducing basal metabolic rate An 800 cal diet only is needed in bed If obesity is present the patient should be maintained on a 1 200 cal diet even after he is up and about This reduces the work of the heart by reducing both metabolism and weight An adequate supply of proteins electrolytes especially potassium and water soluble vitamins all of which may be lost in the diuresis consequent on the improvement of heart failure is important Meals should be taken dry drinking between meals to diminish flatulent *distension*

Oedema increases the venous return and body *weight both of which increase the energy* output of the heart Its removal is of paramount importance The diet must contain only 0 5 g of salt per day and afterwards on return to work a salt poor diet with 2–4 g indefinitely should be given Kempner s rice diet while being very effective in some cases is too unpalatable for most patients and is needless with the other means at our disposal for controlling oedema The most effective diuretics are the organic compounds containing about 40 per cent of mercury those in common use are mersalyl salyrgan neptal and mercaptomerine (Thiomerin) The first three drugs are given intramuscularly or intravenously the last may be given subcutaneously also A test dose of 0 5 ml is given to exclude any idiosyncrasy *and the next morning 2 0 ml is given* It is given in the morning to avoid disturbing the patient s rest by micturition at night The injection is given above the level of the oedema so that it is not diluted by the interstitial fluid where absorption is slow Ammonium chloride 2 g (30 gr) is given the night before the injection and for the following 2 days as the effect of the diuretic lasts at least 36 hr and an acid urine during this time increases its effectiveness A mercurial diuretic should not be *given more often than twice a week cumulative* effects may result in mercury poisoning On occasions cramps diarrhoea and skin rashes result when other diuretics will have to be used If a low salt diet is also used care must be taken that hyponatraemia does not result its symptoms may mimic increasing heart failure and cause death The blood levels of sodium potassium and chlorides need checking if suspicious weakness stupor and tachycardia develop If painful the intramuscular injection may be given with one or two minims of procaine If the response to intramuscular injections diminishes the intravenous route may be used On extremely rare occasions death probably due to ventricular fibrillation has followed intravenous administration The drug must therefore be given by this route slowly and only after the intramuscular route has been tried Catastrophes have occurred only in extremely ill cases and in such sudden death may happen even apart from intravenous injections Mercurial diuretics are as effective in left as in right heart failure and are of great help in preventing nocturnal asthmatic attacks They should be given in diminishing frequency as the oedema diminishes and may be discontinued when little or no diuresis follows their administration They may have to be continued indefinitely in some cases

Acetazolamide (Diamox) causes diuresis by *interference* with the enzyme action in the cells of the renal tubules regulating re absorption of sodium *Its effect lasts over 24 hr* and therefore it need be given every 2 days only Its efficiency diminishes if dosage is too high and intermittent dosage is more effective Chlorothiazide (Saluric) interferes with the re absorption of chlorides and with this of sodium and potassium It is as effective as an injection of a mercurial diuretic One or 2 g of chlorothiazide is given by mouth 4 or 5 days in the week depending on the degree of the oedema Potassium chloride up to 4 or 6 g a day may be necessary if the blood electrolyte balance is disturbed Chlorothiazide also has a hypotensive action and if any hypertensive drugs are being administered at the same time it may be necessary to reduce their dosage Amino

phylline (Theophylline ethylenediamine) may be given by mouth (0 2 g t d s) or as a suppository (0 4 g at night) the latter to avoid gastric irritation To this end it is also combined with various other substances e g aluminium hydroxide (Theodrox) Other diuretics now used with decreasing frequency are theobromine with sodium salicylate (Diuretin) and urea If the latter is used occasional blood urea estimations should be done

Cation exchange resins are given by mouth they prevent the absorption of sodium from the gut and remove it from the intestinal secretions Especial care must be taken that excessive sodium and potassium depletion does not result and the blood levels must be determined regularly Potassium and ammonia are given combined with the resin to avoid hypopotassaemia and acidosis

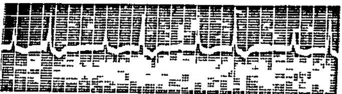
Oedema usually responds to one or more of these measures, but when it is extreme and does not diminish at a satisfactory rate it may be removed by inserting Southey s tubes into the subcutaneous tissues of the feet This is a much more convenient method than acupuncture the amount of fluid can be measured the patient remains comfortable and the skin of the feet does not become sodden from the constant wet dressings Collections in the chest or abdominal cavities usually absorb satisfactorily but they may be removed if they persist In pleural effusions it is as well to remove these soon the increased aeration helping the recovery of the heart When large the effusion is aspirated slowly to avoid inducing an attack of acute pulmonary oedema A rapid means of reducing the work of the heart and one which is extremely helpful in emergencies is venesection Provided that anaemia is absent about 300–600 ml of blood are removed rapidly and this may be life saving on occasions Anti thyroid drugs such as carbimazole are helpful in some cases of chronic right heart failure by producing a mild degree of myxoedema When the cause of failure is removable e g thyrotoxicosis anaemia or arterio venous aneurysm dramatic results may follow its treatment

The efficiency of the heart action is improved by digitalis by removing infection and in the presence of cyanosis by the administration of oxygen Digitalis is obtained from the leaf of the Digitalis Purpurea and contains digitoxin gitalin and gitoxin or from Digitalis Lanata when it contains lanatoside A B and C The basic action of these various constituents is the same they vary in their rate of absorption and excretion and the duration of action on the heart Digitoxin is obtained by hydrolysation of lanatoside A and digoxin by hydrolysation of lanatoside C They act on the failing heart muscle increasing its force of contraction Its efficiency as measured by oxygen need per unit of work produced is improved Digitoxin and digoxin reduce the rate of the heart by vagal stimulation probably by its effect on the carotid sinus and stimulation of the auriculo ventricular node In heart failure they increase the heart output diminish the circulation time improve the urinary output reduce the venous pressure and with this all signs of congestion lessen The slower rate and longer diastole allow improvement of cardiac nutrition

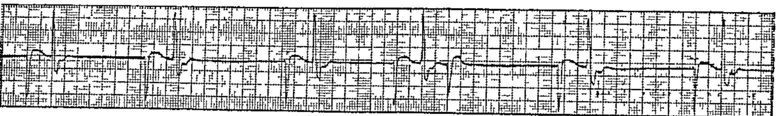
The preparations in common use are digitalis folia digoxin digitalin and lanatoside C (Cedilanid) The advantage of the last three is that they are pure products and their action is more uniform for a given dose They differ in th ir rate of absorption and length of action Lanatoside C and its breakdown product digoxin are absorbed rapidly and rapidly excreted They are of value in severely ill patients when they may be given intravenously if the need is urgent Lanatoside C 1 2–1 6 mg in 6–8 ml or digoxin 1 0–1 5 diluted to 10 ml sterile distilled water is given depending on the build of the patient An effect is seen in 10 min and reaches a maximum in about 1½–2 hr By mouth lanatoside C 6–7 5 mg is needed for digitalization this may be given in divided doses in 24 hr or spread over 2–3 days depending on the severity of the case Digoxin 1½ mg may be administered followed in 6 hr by 1 0 or 0 5 mg depending on the need An effect is seen in 1 hr increasing for the next 6 hr The maintenance dose is 0 25 mg twice daily for both They are excreted rapidly and the patient soon recovers from any toxic effect Digitalis leaf and digitoxin (Digitaline Nativelle) are more slowly absorbed their action is more prolonged and they are more slowly excreted They are thus much more liable to dangerous cumulative effects This applies to digitoxin in particular as it is almost completely absorbed from the intestine and especial care is called for its use The digitalization dose for digitalis folia is 2 0 g (32 gr) and for digitoxin 1 2 mg by mouth This may be given in divided doses in 24 hr or spread over 2–3 days The maintenance dose is about 100 mg (1½ gr) of digitalis folia and 0 2 mg of digitoxin daily Rapid digitalization is never begun unless it is certain that the patient has not had digitalis in any form in the previous two weeks

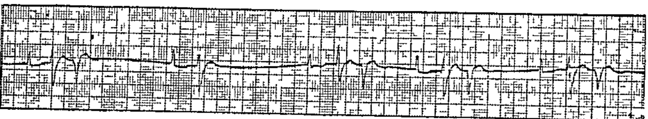
Digitalis is the most effective and valuable drug in cardiological practice and every physician should take great care in its use No two patients react in the same way and dosage has to be cautiously controlled In severe cases the maximum therapeutic effect is gained by dosage which approximates to the toxic dose Used with the other means of con

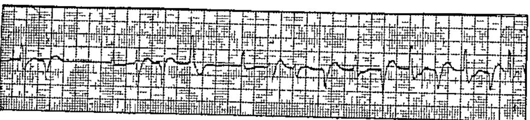
FIG 15 19 HEART FAILURE DIGITALIS INTOXICATION

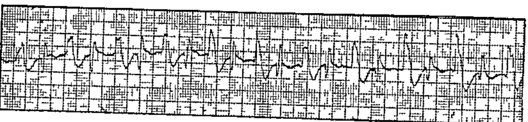


Digitalis Effect P–R interval prolonged coupled beats typical depression of S–T segment









Digitalis Effect Auricular fibrillation bradycardia with coupled beats leading to increasingly numerous ventricular extrasystoles and ultimately ventricular tachycardia the beats originally from R to L ventricles alternately

trolling failure especially rest and removal of oedema toxic effects should rarely be seen

Digitalis first lowers the pulse rate and this should be maintained between 70–80 If the dose is increased it falls to 60–50 when extrasystoles become increasingly frequent Ultimately the rate falls to 40 or below, with complete heart block Regular extra systoles may then occur resulting in pulsus bigeminus By this time salivation nausea and vomiting develop the vomiting being so persistent that dehydration follows Diarrhoea increases this and there is headache confusion of thought or stupor, and occasionally blurred vision or yellow or green vision The extra systoles increase to result in ventricular tachycardia the pulse being very rapid and the blood pressure and urinary output falling Death results from coma or suddenly from ventricular fibrillation Once overdosage has been recognized usually by the slow heart rate and frequent extra systoles the drug is stopped the length of time depending on the particular drug used If digitoxin it may need to be stopped for a week If dehydration or collapse is present rectal or intravenous fluids are given When extra systoles are very frequent potassium or procaine amide hydrochloride are given by mouth or intravenously if ventricula tachycardia is present Digitalis intoxication (see Fig 15 19) is more liable to occur when marked diuresis is occurring as this removes potassium as well as sodium

If a patient has entered failure due to primary myocardial damage he will need to continue with digitalis indefinitely If the cause is removable as in thyrotoxicosis or arteriovenous aneurysm the drug may be discontinued and the effect observed after surgery

Infection often precipitates failure in the elderly and control of this is often sufficient to improve the heart action Any bronchial or urinary infection should be sought for and treated as well as the more obvious causes Oxygen is of use only in the presence of cyanosis but is of great value then It may be administered by nasal catheters (held in position by spectacle frames) by a B L B mask or most effectively by an oxygen tent. These may be borrowed from local hospitals under the N H S

Circulatory Failure

Acute Circulatory Failure

As in chronic heart failure sudden heart failure is present when the output of the heart falls below that necessary for adequate nutrition of the tissues The degree of acuteness of failure determines the resulting clinical picture When very severe sudden death may occur when less rapid sudden loss of consciousness takes place with recovery as compensatory mechanisms come into play when slower still the clinical picture of shock is seen Acute failure may be induced by an inadequate venous return by mechanical obstruction to the blood flow or by myocardial failure

1 *Insufficient venous return* may be caused by

(*a*) Rapid loss of blood or of plasma or of both Examples of this are rapid bleeding from a peptic ulcer or an ectopic pregnancy internally or externally from wounds loss of blood and plasma may occur with burns or injury to muscle masses

(*b*) Pooling of blood in the dilated splanchnic or muscle capillaries and arterioles Reflex or neurogenic vaso dilatation results from severe visceral pain arising in the heart testicles kidneys etc it follows acute inflammation of the pancreas or sudden irritation of the peritoneum when a viscus perforates Peripheral vasodilation is produced from an unduly excitable carotid sinus The pressure of a neck band on twisting the neck or coughing or even the pressure of a razor when shaving may induce light headedness or unconsciousness Vaso dilatation is also produced by hypotensive ganglion blocking drugs and by lumbar sympathectomy Inadequate vasomotor reflex activity in adolescents or convalescents results in a similar postural hypotension Postural hypotension is found in middle aged patients and is described more fully later

(*c*) Haemoconcentration due to fluid and electrolyte loss from the intestine as in gastro enteritis of children and cholera the skin in excessive sweating and the kidneys in diabetes and Addison's disease

2 *Mechanical interference with the blood flow* may be extra vascular as in cardiac tamponade due to haemorrhage or infection or intravascular as with a large pulmonary embolism or a ball valve obstruction of the mitral orifice

3 *Acute myocardial insufficiency* is seen in myocardial infarction or acute myocarditis *e g* diphtheria

When cardiac output falls as a result of these events tachycardia and peripheral vaso-constriction take place as compensatory mechanisms which attempt to maintain the blood pressure and output of the heart The vaso constriction fails ultimately and at death vaso dilatation is found The fluctuating vaso constriction before death causes a similar

change in blood pressure and heart rate which fore tells the end The first group may be called vaso motor insufficiency the second and third groups may be combined as cardiac insufficiency Often elements of both are present *e g* myocardial in farction when severe causes sufficient pain to in duce reflex vaso dilatation

As in chronic failure compensatory mechanisms come into play *i e* tachycardia and peripheral vaso constriction there is no time for others to occur These with the impaired cardiac output, produce the clinical picture of shock

Clinical Picture In the early stages the patient may be restless and agitated with increasing tachycardia increasing pallor and a cold clammy skin The vaso-constriction may be sufficient to maintain the blood pressure at this time Later with falling blood pressure and diminishing arterial blood supply mental apathy and muscular weakness result in a silent still patient with increasing diffi culty in concentration and diminishing interest in his surroundings The skin is grey and may become cyanotic remaining moist with perspiration The pulse continues to rise and become more thready but the blood pressure now falls st adily until it is unobtainable As the blood pressure falls the urinary output is diminished and anuria results Respirations are usually rapid Towards the end the patient may lapse into coma the pulse may fluc tuate the respirations vary and he dies In the early stages the condition may be recovered from but as it advances and the longer it is present, the less cer tain this is A stage is reached when whatever treat ment is given the patient cannot recover he has entered into irreversible shock It is important therefore to avoid conditions leading to shock to recognize it as soon as possible and to treat it vigorously from the first.

Treatment. Diagnosis is essential for proper treatment if known the cause is dealt with Bleed *ing is stopped* diabetes *or Addison s disease treated* etc Morphia in adequate dosage is given for pain intravenously when necessary A horizontal position and elevation of the legs or even binding the limbs as a temporary expedient increases the blood supply to the heart and brain Blood or dextran is given for blood loss and fluids electrolytes and alkalies when needed Sympatheticomimetic drugs such as nor adrenaline and occasionally A C T H or cortisone are needed the latter is helpful in Addison s disease and in severe infections In in fections the appropriate antibiotic is also given

Syncope

Syncope indicates sudden or gradual loss of con sciousness of short duration and spontaneous recovery It is usually due to sudden fall of blood pressure due to peripheral vaso-dilatation and con sequent inadequate blood supply to the brain More rarely it may be due to cardiac causes such as Stokes Adams attack severe tachycardia or aortic stenosis especially when associated with effort

The common faint (vaso vagal syncope vaso motor syncope) is an example of this It occurs in susceptible individuals induced by sufficiently intense psychogenic factors usually apprehension disgust pain or personally intolerable circum stances such as guilt or shame The upright posture a hot atmosphere and fatigue increase the likeli hood of an attack. Its onset is usually gradual enough for the patient to sit down A sense of heat or cold nausea or sinking occurs Vision becomes misty voices fade and consciousness is lost. The skin is cold and clammy or intense perspiration occurs the pulse usually slows and may become im perceptible and the blood pressure falls this last being the cause of the unconsciousness The patient may sit or fall to the ground depending on the speed of the progression of the condition re covery sets in in a few minutes and the patient feels weak and shaky for a little while Recovery is complete

Postural hypotension may occur in some subjects if the upright posture is too long maintained Some middle aged arterio sclerotic patients tend to faint on standing or after meals the complete syndrome includes lack of perspiration and impotence and is believed to be due to vascular lesions in the hypo thalamus This interferes with the sympathetic innervation to the body so that vaso motor reflexes which compensate for changes in posture do not take place and anhydrosis and impotence may also result.

Differential Diagnosis. It is important to differen tiate this from an epileptic attack. In syncope there is a longer warning of the impending attack the *circumstances are usually characteristic and the* description of its progress by onlookers afterwards helps in diagnosis The patient is pale or may be flushed the pulse is usually very slow and feeble but improves as she recovers

In an epileptic attack the aura is short or lacking completely the attack follows a characteristic course but motor activity may be absent There may be a fairly long flaccid stage with evidence of upper motor neurone affection before consciousness is recovered On waking the patient may complain of a muzzy head or severe headache and there may have been micturition or he may have injured him self in falling or bitten his tongue The attack may occur at any time and when the patient may be sitting or lying

Treatment A simple faint is soon recovered from the horizontal position loosening the neck band a cold drink or a cool breeze by stimulating the sympathetic help in recovery Postural hypotension is treated by ephedrine small doses of atropine and sedatives The head of the bed may be kept on blocks so that vasomotor tone in the lower limbs tends to be maintained during the night

Sudden Death

This is often due to cardiac causes It may follow ventricular fibrillation due to myocardial infarction Stokes Adams attack or advanced coronary artery disease Progressive cardiac tamponade due to rupture of the heart or injury can produce it A massive pulmonary embolism may cause it by obstruction to the blood flow or by vagal reflex and cardiac stand still Sufficiently rapid and severe haemorrhage can cause it by lowering the blood pressure Aortic stenosis may interfere with the blood supply to the brain or the heart and syphilitic aortitis may cause ventricular fibrillation by anoxia of the myocardium due to stenosis of the coronary arteries

HYPERTENSION

Hypertension indicates a level of blood pressure above that which is considered usual at the age of the patient It implies the possibility of complications arising in the heart retinae brain or kidneys Hypertensive disease is present when such complications have occurred

The blood pressure varies from patient to patient and in the same patient from moment to moment depending on mental and physical activity emotional stress and such conditions as pain, cold smoking eating and drinking The pressure is usually about 75/40 mm of mercury at birth and rises slowly as age advances reach 100/60 at puberty 120/80 at forty years and 140/90 at sixty years From then on the systolic pressure rises more quickly than the diastolic pressure due to the increasing rigidity of the great vessels These are *basal readings* that is readings taken with the patient relaxed mentally and physically at regular intervals until a steady level is obtained *Casual readings* taken at home or in out patient clinics can be most misleading and on such readings patients may be condemned to needless anxiety and irksome or dangerous treatment

The normal blood pressure is therefore very difficult to define as an arbitrary figure has to be decided upon The pressure varies with age and at any age there is an appreciable scatter of about 10 per cent about the accepted mean The more the reading deviates from the mean the more likely it is to indicate a pathological elevation of pressure Any reading above 150/90 indicates a true hypertension but by no means indicates any need for treatment these factors will be discussed later

Pulse Pressure This is the difference between the systolic and diastolic pressures In systole the large vessels are distended by the stroke volume that is the output per beat of the heart Thus the systolic pressure and therefore the pulse pressure will rise with increased stroke volume and with arterial rigidity Factors increasing stroke volume are exercise emotion arterio venous shunts (including patent ductus arteriosus and Paget s Disea e) aortic incompetence thyrotoxicosis and heart block Arterial rigidity is found with atheroma and associated diseases such as diabetes mellitus and hypertension itself All these conditions are associated with a high systolic pressure The average pulse pressure lies between 40–70 mg Hg It is diminished in aortic stenosis

Mean Blood Pressure This is the average pressure throughout the whole cardiac cycle and depends upon the cardiac output and the peripheral resistance It approximates more nearly to the diastolic pressure which makes the latter reading so important Cardiac output varies with blood volume exercise and emotion The peripheral resistance depends upon the blood viscosity and the elasticity and diameter of the vessels Under normal circumstances the variable factor is the diameter of the vessels controlled by sympathetic and vagal activity and treatment is largely directed to the control of these activities Factors increasing sympathetic tone cause high diastolic pressure

Aetiology About 20 per cent of cases of hypertension have a recognizable cause These are most important some of the causes being removable with cure of the high blood pressure In any patient below the age of forty years and any patient with a history suggestive of these conditions above this age such causes should be sought before treatment is instituted

Renal causes as a group are the most common Acute nephritis is accompanied by a moderate rise in pressure which settles as the condition subsides Chronic nephritis is frequently associated with marked hypertension and in its later stages is indistinguishable from essential hypertension Chronic pyelonephritis is often unsuspected It may be bilateral as when due to obstruction to bladder outflow or unilateral Ureteric catheters may have to be passed to decide this and to determine what

function remains in the unaffected kidney if the condition is unilateral It may respond to chemo therapy If severe renal atrophy has occurred and the unaffected kidney function is adequate removal of the affected organ may result in cure Rarer causes are polycystic kidneys periarteritis nodosa and unilateral renal lesions due to arterial or venous obstruction by thrombosis or pressure or arterial emboli

Toxaemia of pregnancy is common It may be due to the pregnancy (pre eclampsia or eclampsia) or pregnancy may occur in a hypertensive patient or in a person with chronic nephritis In the great majority of cases the blood pressure returns to its former level but in a few it remains persistently raised and in chronic nephritis the kidney function may be further impaired

Endocrine causes are very uncommon but their importance lies in their being amenable to treat ment. Phaeochromocytoma of the adrenal medulla may cause severe paroxysmal bouts of hypertension or may result in a sustained hypertension indistin guishable from essential hypertension The rise in pressure is due to the increased secretion of adrenaline and nor adrenaline These may be esti mated quantitatively in the urine adequate rise in amounts being diagnostic The site of the tumour is found by intravenous pyelography or insufflating air into the pre sacral region which then rises to outline the kidneys and supra renals Hypertension associated with Cushing s Syndrome (basophil adenoma of the pituitary or adrenal adenoma) is due to the retention of sodium and water Sodium retention is probably the cause of the hypertension in toxaemia of pregnancy and acute nephritis also

Co-arctation of the aorta is a congenital condi tion which results in hypertension by diminishing the blood supply to the kidneys hypertension does not occur if the aortic narrowing is distal to the origin of the renal arteries

Essential Hypertension

In the remaining 80 per cent of cases no cause can be found for the rise in blood pressure and the condition is called essential " It is very common its incidency increasing with age so that three quarters of the population are hypertensive over 70 years of age It usually begins to be associated with symptoms between the ages of 40 and 60 but its origin occurs long before this Its rate of progress varies when slow it may be accompanied by no symptoms during the lifetime of the patient when it is called benign hypertension when rapid it may cause death in 6–12 months when it is known as malignant hypertension The latter is rare account ing for only about 2 per cent of all cases of hyper tension it occurs 3 times as commonly in men as in women Benign hypertension is found equally in men and women rather more frequently in males in the upper classes in women in the lower classes

Heredity is most important. It has been shown that if neither parent has hypertension their children have a 3 per cent chance of acquiring it if one parent is hypertensive the children have a 30 per cent chance while if both parents are hypertensive their children have a 45 per cent chance of being hypertensive

High blood pressure readings as measured by the cuff method are frequently due in obese persons to the extra pressure needed to compress the upper arm and the escape of the bag from beneath the cuff if not carefully applied There is no proof that obese persons suffer more frequently from hyper tension than others but obese persons with hyper tensive heart disease have a higher mortality due to the increased work of the heart. The person of thick set florid constitution is more frequently affected than the slender lean type but any build may be affected Nor is there a classical motional type of hypertensive patient Suppre d anger quiet ambition or colourful display of the emotionally labile may each be seen associated with this condi tion It is found however that labile hypertension with undue rises of pressure under stress more often develops into a sustained hypertension as time passes

Essential hypertension is considered to be a dis- ease of civilization Africans rar ly develop it, but town bred American negroes suf er equally or more frequently from it than white Americans

Pathogensis The precise c use of essential hyper tension is still not known despite an enormous amount of work done over many years in many countries The cardiac output, blood volume and blood viscosity are all normal the rise in pressure being due to increase in the peripheral resistance by arteriolar contraction How much is due to neurogenic and how much to humoral activity is undecided Immediate vaso-constriction is brought about by nervous reflexes from the aortic arch and carotid sinus when the pressure falls in these vessels a longer action is seen in sustained stre Even after hypertension has been present for ma y years and structural changes have occurred in the artery walls lowering of pressure is possible with ganglionic blocking drugs The effect of adrenaline and nor adrenaline is seen in the hypertension associated with phaeochromocytoma

Humoral agents have been isolated in the blood of human hypertensive patients with acute nephritis and pre-eclampsia also in experimental animals

These disappear if hypertension is present for a con siderable time so that it is not found in patients with essential hypertension They are formed in the kidney when its blood supply is diminished (the Goldblatt experiments) The enzyme renin is secreted which acts on hypertensinogen a globulin formed in the liver to produce hypertensin which causes contraction of the arterioles Hypertensin is destroyed constantly by hypertensinase an enzyme present generally in body tissues In animals it has been possible to produce an antibody to renin but this has so far not been done in man The degree and rate of progress of the hypertension can be increased experimentally by increasing the degree of renal ischaemia If severe enough the rate of forma tion of renin is greater than the rate of its destruc tion or excretion and a vicious circle results producing malignant hypertension and a rapidly fatal outcome This explains the improvement obtained when a single diseased kidney is removed the other being normal Another system of enzymes is also described a vaso excitor material formed under similar conditions having its effect distal to the arterioles wh ~h is opposed by a vaso depressor material formed i the liver and skeletal muscles It is probable that i man the original changes are caused by sympathetic over activity that produces sufficient renal ischaemia to maintain the hyper tensive state by humoral agents

The last factor which must be mentioned is the influence of the adrenal cortex on retention of sodium and fluids This results in a rise in blood pressure as in Cu ung s syndrome and probably in acute nephritis an.l toxaemia of pregnancy The exact mechanism is ot known but it leads to an increase in periphera resistance and therefore in the blood pressure

Clinical Picture As stated earlier persons whose blood pressure rises unduly under stress or such stimuli as cold tend to develop a sustained hyper tension These early stages are quite symptom free indeed symptoms may not arise until complications have arisen and then they are related to the system involved The complaints associated with hyperten sion are common to anxiety states in general and may develop only after the patient has been told that the bl(od pressure is raised Then headache dizziness ea y fatiguability lack of concentration and insomnia occur The headache is characteristic of anxiety a tight feeling round the head a pressure or boring sensation at the vertex usually worse towards evening when resting after a day s work It may however consist of a dull heavy ache or throbbing in the occipital region present on waking in the morning and wearing off in a few hours after getting up This may occur when the patient has no knowledge of his hypertension and the cause is not definitely known It is not relat d to the cerebrospinal fluid pressure or the degree of hypertension it may never occur in some patients whose pressure is extreme

Hypertension is thus usually discovered at routine examination as an unexpected finding Its rate of progress may be slow moderate or catastrophic The earlier benign forms may continue for ten to fifteen years before complications occur The last malignant form may occur at any age in the course of hypertension due to any cause and produce death in a few months or at most a year It most com monly occurs in the fourth decade In some cases it arises without any precipitating cause in persons whose blood pressure was known to have been normal It is undecided whether its aetiology is distinct from that of the benign form or whether it is merely an extremely rapid form of the same condition

Complications The rate of progress and develop ment of complications depend in general on the level of hypertension and the length of time it has been present Marked exceptions may o cur how ever They affect in particular the heart brain re tinae and the kidneys but of course the whole arteriolar system is affected the results being most evident in these organs

The Heart As long as the left ventricle can cope with the added load the cardiac reserve heart size and electrocardiogram remain normal Gradually the effects are recognizable clinically Increasing dyspnoea on effort becomes evident until episodes of left ventricular failure occur Orthopnoea and paroxysmal nocturnal dyspnoea disturb rest with increasing frequency Once left ventricular failure has occurred it is unusual for life to continue for much longer than eighteen months Often death occurs more rapidly and if the heart is very large it may happen at any moment due to ventricular fibrillation Ultimately the right ventricle fai's in its turn with all the signs of systemic congestion Hypertension is very commonly associated with coronary artery disease and angina pectoris and cardiac infarction are frequently encountered The heart size remains normal for years but ultimately hypertrophy takes place (*see* Plate 15 2) As failur of the left and later the right ventricle develops dila tation as well as hypertrophy takes place and the heart attains an enormous size These changes may occur relatively rapidly after years of active lif with sustained hypertension With failure the level of the blood pressure falls first the systolic and later the diastolic so that the pulse pressure is most affected The apex beat is displaced downwards and outwards with the hypertrophy and a gallop rhythm

develops most marked once failure takes place Alternation of the pulse may be felt or recognized during the taking of blood pressure With failure of the left ventricle crepitations develop at the bases where effusions may begin to collect. With failure of the right ventricle systemic venous congestion occurs This may be present without evidence of left ventricular failure and the lung fields may be normal (Bernheim s syndrome) It is possible that the concentric enlargement of the left ventricle en croaches on the cavity of the right ventricle causing a functional stenosis of the tricuspid valve with resultant production of right ventricular failure The heart size the pulmonary congestion and the pleural effusions are seen on radioscopy The elec trocardiogram remains normal until hypertrophy occurs when widening of the QRS complex de pression of the S T segment and inversion of the T wave occur

The Brain In the lay mind hypertension is associ ated with strokes and sudden death these fears are the cause of numerous symptoms referable to the central nervous system The anxiety headaches dizziness lack of concentration and fatiguability already referred to are the result As the condition lasts longer however arteriosclerosis of the cerebral vessels may develop This results in similar symp toms True vertigo may develop however with tin nitus when the vessels to the inner ear are affected Diplopia follows kinking of the internal carotid artery in the cavernous sinus which may clear spontaneously after a few weeks A general falling off in mental ability may follow numerous minute thromboses or pseudo bulbar palsy may result When larger arteries are affected thrombosis or haemorrhage may occur These may be preceded by transient symptoms of headaches weakness para esthesia or visual or speech defects Similar prod omata are experienced before an attack of so called hypertensive encephalopathy In this however a sharp rise in blood pressure accompanies the event and consciousness is often lost for minutes hours or even a day or two On recovery no residual cerebral damage is found clinically although the longer the attack lasts the more likely is this to have occurred In most cases a thrombosis has occurred with vari able oedema the signs clearing as the oedema diminishes The diagnosis is arrived at by excluding any other cause of transient unconsciousness It must be remembered that hypertensive subjects are also liable to such conditions as cerebral neoplasms epilepsy uraemia and lead poisoning

The Eye By retinoscopy a direct view of the arterioles is obtained changes here reflect the general arteriolar state throughout the body and supply us with very valuable information

These changes may be more informative than the actual level of the blood pressure reflecting a more exact condition of the general state of the arterioles In hypertensive disease the easiest change to recog nize is the irregular calibre of the arterioles but a somewhat earlier change is a narrowing of the arteriole compared with the vein The normal ratio of artery to vein is 4 5 but as the arterioles become narrowed this alters Four grades of retinal change have been described each carrying a progressively more serious prognosis In Grade 1 narrowing of the arterioles is present This is more marked in Grade 2 and there may be old hard exudates Fresh haemorrhages and exudates are seen in Grade 3 with oedema of the retina generally In Grade 4 swelling of the disc head is present When this occurs malignant hypertension is present and death usually occurs within six to twelve months These changes are also seen in chronic nephriti and as temporary changes in acute nephritis and toxaemia of pregnancy retrogressing as the condition im proves The haemorrhages may be small linear or flame shaped when superficially placed on the retina or may raise the retina as a plum coloured swelling when more deeply placed Detachment of the retina or haemorrhage into the vitreous may also occur The patient complains of increasing difficulty of vision ending in blindness varying in its rate of progress from patient to patient

Eye changes are found in arteriosclerosis without hypertension these are an increase in the light reflex from the artery increased tortuosity and thickening of artery walls and kinking and obstruc tion of the veins at the intersection of artery and vein These are not related in any way to the level of the blood pressure

The Kidney In benign hypertension the renal function is not affected for many years and then only to a slight degree usually in proportion to the arteriosclerotic changes which take place with long sustained hypertension The renal blood flow is diminished and a trace of albumin with an occa sional hyaline cast is found renal failure is very rare In malignant hypertension however uraemia is the commonest cause of death The urine is loaded with albumin hyaline and granular casts are present and the blood urea rises steadily with all the con comitant findings of this condition These changes usually follow papilloedema but rarely renal failure with heavy albuminuria may precede the retina changes of malignant hypertension When the hyper tension is secondary to renal disease the presence of casts and albuminuria occurs in the early stages of hypertension but if malignant changes occur the conditions seem identical Only about 10 per cent of patients with hypertension die from renal failure

Prognosis *It is first necessary to decide whether* a casual reading above normal represents a sustained hypertension especially if only slightly or moderately high To decide this it may be necessary to take repeated readings with the patient in bed or perform a sedation test For this he is given amylobarbitone (Amytal) 0 2 g (3 gr) at hourly intervals for three doses the pressure being taken at half hourly intervals until it begins to rise

Prognosis depends upon the family history sex obesity the presence of renal disease or other specific cause for hypertension and the presence of complications If there is a strong family history of hypertension the condition is usually steadily progressive at a more rapid rate than if such a history is not present Females stand the condition better than males Obese persons live longer than thinner people with hypertension perhaps because of the misleadingly high readings obtained by the cuff manometers Search must always be made for causes of hypertension amenable to treatment especially in people under forty years of age Coarctation of the aorta unilateral renal disease due to congenital lesions pyelonephritis tuberculosis hydronephrosis or stones may be treated surgically and infections by the appropriate antibiotic or chemotherapy Polyarteritis nodosa may be controlled by cortisone and phaeochromocytoma removed So long as the heart kidneys retinae and brain remain normal the patient may live a normal span of life Once complications begin to occur the outlook deteriorates These are commoner the higher the level of blood pressure but this does not necessarily apply on occasions complications develop rapidly when the level is only moderate while in others they may live a surprising length of time with a severely raised pressure Once hypertension has been diagnosed regular annual checks should be made noting especially changes in the four sites mentioned The rate of incidence and progress of these complications give an accurate guide to the future expectation of life

Treatment The cause of hypertension not being known no specific treatment can be given In recent years very effective drugs have been used with good results but they may also produce dangerous complications and unpleasant side effects

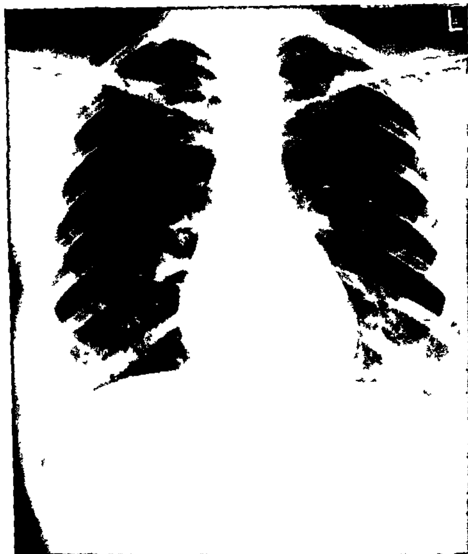
If hypertension is found in a symptom free patient he is told of this to offset any alarm he may feel if it is found and unduly stressed by another doctor It should be mentioned as an incidental finding and the patient reassured and advised to continue his work provided it is not unduly strenuous and to play games if they are not team or competitive Diet is not restricted unless obesity is present and no drugs should be given If the patient is under forty years of age search should be made for a possible removable cause If the level is high e g 200/110 he should be examined at yearly intervals It should be impressed on him that no complication is likely to arise for many years the examinations giving warnings of these and indications for treatment in due course

Obesity should be treated often this is sufficient to bring the pressure down without need for other treatment A low salt diet is a valuable means of treatment but unless it is rigidly adhered to for a considerable time results are poor Less than 1 g of salt a day is necessary in the diet, and unless this can be achieved it is useless to give a low salt diet at all

Bowel action should be easy avoiding strain Adequate rest is most important In the early stages 9 hr bed rest at night half an hour after meals and lazy week ends should be indulged in Prolonged hours of work should be avoided unnecessary commitments dropped and the patient s activities so spaced that he is able to relax between them Sedatives are given to assist relaxation and help to remove anxiety

In the past numerous drugs have been employed in an attempt to reduce the blood pressure but apart from potassium thiocyanate none were effective except as a placebo Nowadays however far more effective compounds are available These are used if complications begin to appear that is malignant hypertension angina or heart failure renal decompensation or the symptoms or signs of cerebral thromboses It is still debatable whether one should give hypotensive drugs to a symptom free patient with hypertension There is no clear evidence on this question as no prolonged series has been followed indeed such a series would be very difficult to assess It is reasonable to treat those whose *pressures continue to rise despite* treatment already described or whose diastolic pressures remain at 120 mm mercury or above and who are young or middle aged The development of complications at any age would justify treatment

Rauwolfia Serpentina (purified extract reserpine Serpasil) acts centrally probably on the higher centres and hypothalamus to reduce the s
thetic activity It is not effective in severe
results are uncertain in milder cases
sedative action and occasional
treme depression with suicida
more effective in conjunction
sive drugs especially the gar
—it levels out their effects ar
the constipation they may ca
alone in mild cases starting w
increasing but never going at



Constrictive Pericarditis with Widespread Calcification of the Pericardium



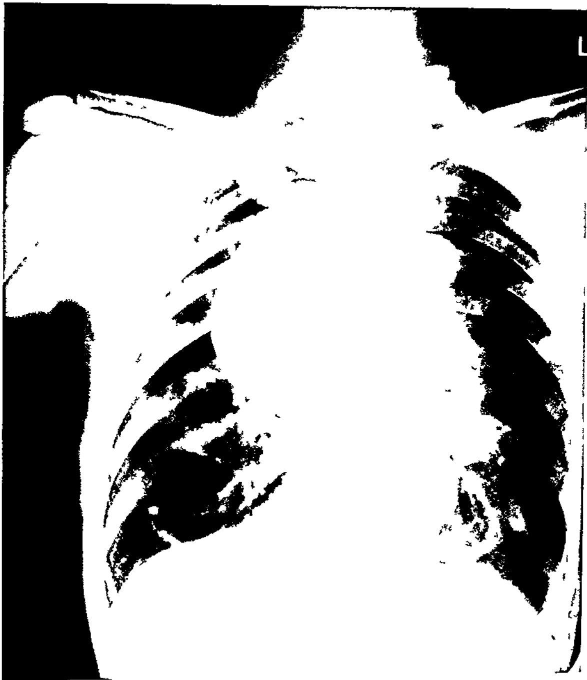
Constrictive Pericarditis with Widespread Calcification of the Pericardium



Syphilitic Aortitis A Saccular Aneurysm of the Ascending Aorta not Affecting the Aortic Valve or the Size of the Left Ventricle

X ray taken 11th June 1952

Plate 15 5



SYPHILITIC AORTITIS SAME PATIENT AS PLATE 15 5
X ray taken 4th March 1958

membering that it may take three to six weeks to gain its full effect Veratrum compounds stimulate the vagus with resulting fall in blood pressure Un pleasant side effects are nausea vomiting hypo tension and bradycardia Tolerance is rapidly gained and there is a small difference between its hypotensive effect and the dose which induces vomiting so that it is not often used. Hydrallazine (Apresoline) acts peripherally causing relaxation of the smooth muscle in the arteries. Twenty five mg may be given two or three times a day gradually increasing to 50 mg t d s or 75 mg t d s It is used in conjunction with other drugs e g ganglion blocking agents

Ganglion blocking drugs cause hypotension by paralysing the sympathetic nerves to the arterioles and are very effective They seem to act on those nerves that are most stimulated so that their effects in hypertensive patients are most marked on the arterioles Unfortunately they also act on the para sympathetic nerves with such unpleasant side-effects as constipation or even paralytic ileus dry mouth paralysis of accommodation and interference with bladder control and severe hypotension Pento linium tartrate (Ansolysen) may be given two or three times a day after meals to ensure even absorption and to avoid sudden falls in blood pres sure It is often combined with reserpine or hydral lazine the combined action being greater than either alone Mecamylamine (Inversine) may be given 2 5 mg b d slowly increasing the dose until control is obtained Absorption is more uniform and com plete and the dosage much smaller than that of the previously mentioned drugs and results are usually very good. Side effects still occur however especi ally constipation These side effects of all ganglion blocking drugs are partly controlled by pilocarpine 3 mg (1/20 gr) t d s and neostigmine 15 mg t d s together with aperients

In view of the variation in dosage the severe side effects and the need for investigation of the patient these drugs should always be started in hospital If the blood urea is above 100 mg per cent these drugs should not be used they cause a rapidly increasing uraemic state Between 70–100 mg per cent, great care should be taken the blood urea being estimated daily the blood pressure should not be lowered to 180 systolic until it is certain that the kidney func tion is maintained

Chlorothiazide hydrochlorothiazide and fluo-hydrochlorothiazide have a considerable hypoten sive action (probably due to a reduction of plasma volume) as well as being diuretics One of these drugs combined with reserpine is often sufficient when hypertension is moderate In more severe cases one of them may be combined with meca mylamine the dosage and side effects of mecamyla mine thus being reduced

Recently new compounds have been used, such as bretylium tosylate (Darenthin) which act by inhibiting sympathetic activity peripherally Its chief advantage lies in the absence of the side effects due to para sympathetic paralysis Its rate of absorp-tion however is variable and with high doses sud den and dangerously severe hypotensive attacks are possible with on occasions fatal consequences These may be combated with adrenaline It may produce parotid pain an oppressive constriction in the chest and other side effects which necessitate its withdrawal It is not as effective as the ganglion blocking agents in severe cases but it can be used in conjunction with hydrochlorothiazide or meca mylamine

Before the introduction of effective drug therapy a fall in pressure was obtained by removal of vary ing amounts of the sympathetic chain More recently the adrenal glands have been removed replacement therapy by cortisone then being neces sary The patient should not be over fifty years old or have had a coronary thrombosis Angina malig nant hypertension and cerebral thrombosis are no bar to operation Young people who respond badly to medical treatment or do not continue treatment correctly make suitable candidates for surgery

ISCHAEMIC HEART DISEASE

Under this heading are described the conditions which arise when the heart receives an insufficient supply of blood for its immediate needs Temporary or permanent changes occur which may be indis tinguishable clinically These conditions have be come increasingly common since the beginning of this century and the rate of increase is accelerating It was only in 1912 that a clear account of clinical cardiac infarction was given and the diagnosis was uncommon until the 1920 s With clearer under standing of the cause of the condition recognition of the variations in symptomatology and especially the increasing use of the electrocardiograph more precise diagnoses are made Precision is essential, as an incorrect diagnosis of this grave condition can convert a normal individual into a cardiac neu rotic while to miss the diagnosis is possibly to court disaster

Aetiology Adequate nutrition of the heart muscle depends upon (*a*) the supply of blood and (*b*) the needs of the heart.

(*a*) The supply of blood is determined by the state

of the coronary arteries the pressure within them and the state of the blood itself

Arteriosclerosis of the coronary arteries is almost invariably found in ischaemic heart disease *indeed the terms are almost synonymous* Its incidence and degree increase as age advances It was as prevalent fifty years ago as it is today *so that it does not* itself account for the increase *in ischaemic heart* diseas For this arterial narrowing or *occlusion is* needed This may be produced by fibrin *deposition* the formation of an atheromatous ulcer with consequent thrombosis or haemorrhage into an atheromatous plaque

The intra arterial pressure *is lowered in aortic re*gurgitation during diastole *which is shortened* characteristically in this condition due to tachycardia *In aortic stenosis* the high intraventricular systolic pressure so compresses the coronary arterioles that circulation ceases during this phase of the cardiac cycle *With both these valve lesions* the heart is also hypertrophied In syphilitic aortitis *gummatous narrowing of* the coronary vessels as *they arise from* the aorta lowers the pressure within them thus diminishing the blood supply to the heart though the arteries are usually remarkably healthy In the tachycardias the blood pressure is lowered and diastole is shortened both factors diminishing the blood flow Haemorrhage and shock have the same effect

The effect of the blood is seen in anaemia which can produce anginal pain when coronary artery disease is present disappearing on correction of the anaemia Hypoglycaemia may produce angina or infarction Prolonged hypercholesterolaemia tends to produce coronary artery disease as does diabetes

(*b*) The work of the heart depends on the size of the heart and its energy output these being interdependent to a certain extent. The energy output is raised in exercise emotion and hypertension Valve lesions usually aortic but occasionally mitral may cause angina thyrotoxicosis is occasionally associated with angina but rarely with infarction The high cardiac output found with anaemia arteriovenous anastomoses and after a meal may be the cause of angina A summation of factors may result in angina the classical example being an obese man with coronary artery disease walking uphill against a wind after a meal and anxious or enraged for any cause

Although hypertension is often associated with ischaemic heart disease this is by no means always present

The incidence of ischaemic heart disease increases as age advances and is highest in the fifth and sixth decades There is a very strong hereditary tendency which behaves as a dominant Males predominate below the age of 70 when the incidence becomes equal in the sexes There is a strong clinical impression *that it is more frequently found* among the *professional and* executive classes This may be related *to the dietary fat* content which usually rises as one s income rises This leads to intermittent rises in blood cholesterol levels which increases the *tendency* both to atheroma and blood clotting *Oestrogens lower the blood cholesterol* which may *account for the freedom of women* below the age *of 40 from angina*

Pathology The results of narrowing or occlusion of a coronary artery depends on its site its rate of narrowing and the state of the remaining arteries Minute anastomotic vessels are normally present, but are quite inadequate to preserve the life of the threatened myocardium if a sudden arterial obstruction occurs Gradual ischaemia stimulates their formation so that a small artery slowly closing may not result in injury If a sufficient numb r close the anastomoses become inadequate so that scattered necrosis followed by fibro is results This leads to progressive left and later right ventricular failure without necessarily any recognizable episode o curring At some point along this course however angina of effort usually occurs and ventricular fibrillation during effort is possible More rapid closure of a larger artery causes clinically recognizable infarction The site of infarction may not corr s pond to the artery closed this will d p nd on the anastomoses present and the position of the myocardium whose needs are critical Sudden closure of one of the main vessels may cause fibrillation and death results before any of the changes usually associated with infarction have occurred Thus it is seen that thrombosis of a vessel may occur without infarction also as a result of narrowing of a sufficient number of arteries layers of the myocardium may die without thrombosis having occurred Coronary thrombosis is not therefore synonymous with cardiac infarction and infarction may occur without thrombosis

Other less frequent causes of obstruction to coronary vessels are periarteritis nodosa haemorrhage into an atheromatous plaque and emboli as from subacute bacterial endocarditis

Angina of Effort

When ischaemia is short lived and reversible angina of effort results

Clinical Picture The cardinal symptom of cardiac ischaemia is pain The heart is supplied by the first four or five dorsal sympathetic nerves and this determines the area of distribution of the referred pain It occurs in the mid line deep to the sternum usually in its central third but it may arise in or

spread to its upper or lower parts or to the epigastrium It may also be referred to the shoulder axillae between the shoulder blades posteriorly or to the arms Both arms may be affected or the left only less frequently the right only It may be felt in the throat jaws teeth or posterior pharyngeal wall It may be experienced at the peripheral areas of distribution first and only later if at all be felt in the chest In quality it is constant pressing crushing aching or bursting but never pricking or stabbing Occasionally it is a burning pain or a hard boring pain or likened to an intense indigestion Often the patient has difficulty in describing it precisely The relationship of the pain to effort is of the first importance If it arises constantly after a certain amount of effort under comparable conditions having the site and quality described then it is angina of effort The fact that it arises first in the hand elbow throat or jaw should not mislead one It gradually increases in intensity as the effort is persisted in and forces the patient to cease then it slowly wanes It continues for about 3–5 min as a rule and rarely lasts more than 10–15 min During this time the accumulated metabolites which cause the pain are removed by the coronary circulation If the pain lasts longer infarction has probably occurred In some cases if the effort is continued the pain slowly disappears and does not reappear despite moderately severe exertion—the so called first wind angina Work to which the patient is accustomed seems to produce the pain less quickly than that to which he is not used The pain is usually constant in its onset but alterations occur due to the variable factors affecting the nutritional needs of the heart muscle

Diagnosis depends entirely on the history On examination and radioscopy the heart may be normal the electrocardiogram however usually shows at least minor changes of coronary artery disease These changes may be increased by effort or breathing 10 per cent oxygen but this is not done unless doubt exists about the diagnosis

Differential Diagnosis The site and quality of the pain and above all its precise relationship to effort usually makes the diagnosis clear In a few cases however after complete investigation doubt still remains It is then advisable to reassure the patient review the symptoms at intervals and note the response to treatment Anxiety states often produce a sense of weight or dragging in the left inframammary region sometimes eased by firm pressure These are described more fully under Cardiovascular Symptoms of Psychogenic Origin (p 290)

Affections of the digestive tract which may cause suggestive symptoms are oesophagitis hiatus hernia peptic ulceration and gall bladder dyspepsia The quality of the pain its relationship to posture diet and meals its relief by appropriate treatment and radiographic aids will help in diagnosis The last two conditions are often associated with coronary artery disease and special care should be taken to distinguish between cardiac and dyspeptic pain

Irregular contractions of the lower end of the oesophagus can cause pain of true anginal quality and distribution when it is virtually impossible to distinguish between this condition and true angina It is not precisely related to effort however and the electrocardiogram is not affected unless coronary artery disease is also present

Pain of skeletal origin may be referred from the inter spinous ligaments and joints to the chest wall and down the arms It may be produced by movements of the spine or develop in certain positions as when reclining in an armchair It can be reproduced by appropriate manipulation of the spine and is alleviated by physiotherapy X ray of the spine may show arthritic changes which however may not necessarily be the cause of symptoms Distressful breathing is caused by inadequate aeration of blood by the lungs it is therefore found in asthma emphysema pneumothoraces or pleural effusions The dyspnoea and chest discomfort on effort may suggest angina but the quality of the discomfort is different and its site is diffuse or along the diaphragmatic attachments

Prognosis The larger the heart the higher the blood pressure and the more the electrocardiogram deviates from the normal the worse the prognosis

Once angina has occurred sudden death from cardiac infarction or ventricular fibrillation is possible Usually pain is more easily induced as time goes on the patient living on an average 10 to 15 years Cases have survived from 20 to 25 years Sudden deterioration follows each infarction which may occur at intervals Alternatively with increasing fibrosis the cardiac reserve gradually diminishes and the patient develops cardiac failure when the pain ceases Angina may also disappear after infarction due to death of the muscle causing the pain

Treatment Angina of less than 6–8 weeks duration especially if increasing in severity or when prolonged attacks occur without adequate cause often presages cardiac infarction This should be treated by 3 weeks rest in bed and the giving of anti-coagulant drugs Time is thus given for anastomoses to form and so improve the blood supply to the threatened myocardium In established angina energy output should be kept within the capacity of the myocardium by increasing the blood supply to the heart and curtailing effort Long acting vaso

dilators such as penta erythritol tetranitrate (Mycardol) 30 mg 3–5 times a day, are given which diminish the ease of production of the pain For the pain more rapidly acting drugs are used Glyceryl trinitrin 0 5 mg (1/100 gr) is placed under the tongue, and dissolved in the mouth In true angina, this relieves the pain and is a valuable point in differential diagnosis (*see* Fig 15 20) If necessary, the dose may be repeated in 10 to 15 min rise in blood lipoids following a fatty meal Constipation should be corrected In severe cases attacks may follow the slightest movement, even turning over in bed In such cases work is diminished by inducing myxoedema by anti thyroid drugs *e g* carbimazole If this induces relief radio-active iodine may be tried Failing this alcohol injection of the upper dorsal sympathetic ganglia is tried. This may bring about great relief with apparent

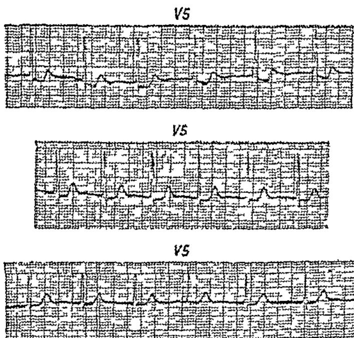


Fig 15 20 Coronary Artery Disease

Ischaemic changes reversed by glycerol trinitrin in five minutes Auricular fibrillation is present

Palpitations and flushing occur as side effects and the patient should be warned about this as they may occasion alarm If the number of attacks warrants it the drug may be taken hourly Its effect does not diminish and the patient should come to regard the drug as part of his routine allowing him to lead as normal a life as possible It may be taken before undertaking effort which may induce an attack of pain

Effort that may induce pain is diminished in as many ways as possible Work should not entail sustained effort or a crowded time table If necessary commitments must be shed or the occupation changed Sedatives such as amylobarbitone 30 mg (½ gr) b d are given to diminish anxiety but the dose needs to be regulated to avoid depression

Hypertension should be brought within reasonable levels Obesity should be reduced by dieting A diet low in fats helps in this and diminishes the increase in effort tolerance of the heart Attempts at directly increasing the blood by surgical means have been tried as by anastomosing the omentum to the myocardium or the parietal to the visceral pericardium and more recently by direct arterial anastomoses to the heart muscle These last methods are in the experimental stage and no definite conclusions have been reached

Acute Coronary Insufficiency

This term is sometimes used to describe a condition more severe than angina but not amounting to clinical infarction Its aetiology is the same as that of ischaemic heart disease in general though it is not always associated with coronary artery disease and may be brought on by such predisposing causes as acute anaemia shock or pulmonary embolism

As the term implies there is insufficient oxygen

for the heart s needs If this is present for a short time the condition like angina is reversible The longer the ischaemia persists the more likely it is that scattered sub-endocardial necrotic foci will result in the papillary muscles and in the left ventricle generally these being subjected to the greatest pressure in systole As the vast majority of cases recover one is left in doubt about the permanent effects

Clinical Picture Usually there is a clear reason for the attack which is marked by anginal pain that lasts longer than the customary 5–20 minutes It is the length of the attack that distinguishes it from angina It differs from cardiac infarction by the absence of fever and leucocytosis The electrocardiogram is characteristic showing depression of the S T segment and inversion of the T wave over the left ventricular leads These changes last for hours or days unlike the more readily reversible ones found in angina The longer these changes last the more likely it is that actual necrosis and not merely ischaemia alone has taken place Although pain is usually the prominent symptom it may be absent the condition being discovered by electrocardiography

Treatment The precipitating cause should be treated and the case supervised like that of an impending cardiac infarct

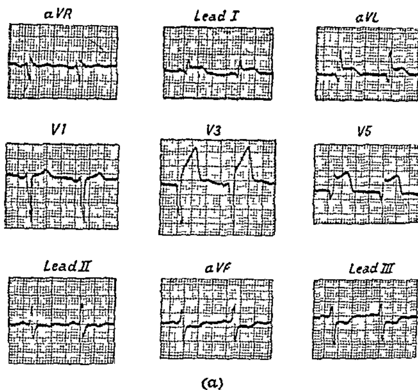
Coronary Thrombosis

When ischaemia is sufficiently prolonged death of mycardium results if great enough in amount the condition is recognizable clinically and is customarily called coronary thrombosis As has been explained already coronary thrombosis does not necessarily result in necrosis and necrosis may occur without coronary thrombosis

Clinical Picture The symptoms range from such slight sensations that they are overlooked to an overwhelming disaster which causes sudden death In most cases the patient has suffered from angina of effort which has steadily increased in ease of onset and intensity this may have been present for so short a time that it has to be sought for carefully in taking the history The pain may not have been typical in that it occurred at rest and lasted longer than the usual anginal pain When infarction occurs the pain gradually and steadily increases in intensity until it can hardly be borne In other cases it comes quite suddenly like a bolt out of the blue Unlike the still silent sufferer with angina the patient is often driven to urgent restlessness in his efforts to find comfort from his agony This together with a sustained blood pressure and absence of electrocardiographic changes in the first 12 to 24 hr may be very misleading indeed there may be a rise in blood pressure initially The patient soon appreciates the difference from his usual anginal pain and customary remedies no longer bring relief It lasts for at least half an hour usually several hours or in very severe cases a day or more it may recur at intervals if the condition continues to spread It has the same quality and distribution as that of angina but is usually much more intense

Immediate shock due to vaso vagal impulses occurs and may be so extreme as to cause unconsciousness or on rare occasions sudden death In severe shock the pain is not always intense and weakness faintness giddiness or unconsciousness are present The blood pressure falls and peripheral vaso-constriction causes pallor with or without cyanosis The skin is cold and clammy or there may be marked perspiration Nausea with vomiting which may be distressing adds to the discomfort The low blood pressure perspiration and vomiting with consequent poor fluid intake leads to oliguria or anuria which is recovered from spontaneously as the shock passes off When the myocardial damage is extensive left ventricular failure or congestive heart failure occur After a slight attack with few symptoms the patient seems none the worse after a few days and little notice may be taken of the short indisposition A more serious attack leaves him feeling ill and weak with easy dyspnoea for a week or more and he slowly regains strength in the next 2 or 3 weeks He may develop typical angina of effort In still more severe attacks he may remain in a state of shock for days and despite all treatment may gradually enter into progressive heart failure and die in several days or weeks

The patient is anxious and restless usually with some degree of shock In vaso vagal shock the pulse is slow the blood pressure low and the skin moist pale or cyanosed He may recover surprisingly quickly from this in 24 to 36 hr More usually the pulse is rapid and the blood pressure begins to fall in 12 to 24 hr depending on the size of the infarct it may continue to fall for the next few days Within a week however it rises to approach its former level With larger infarcts the fall continues for a week or more and is correspondingly greater the rise is slower and the final pressure well below its original level The temperature rises in 24 hr usually to about 101 and remains raised for a few days or a week there is an accompanying rise in white blood cells and serum transaminase The E S R rises in a few days and remains raised for four to six weeks The temperature W B C and E S R are some measure of the amount of muscle damaged The heart sounds may be normal but are usually muffled and faint and in severe cases a gallop rhythm is heard over the left ventricle



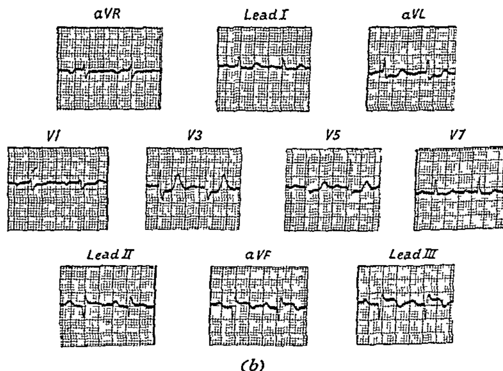


FIG 15 21 CORONARY THROMBOSIS

(a) Acute antero lateral infarct
(b) Acute posterior infarct

Occasionally in about 10 per cent of cases a pericardial friction rub is heard which may be quite evanescent and is not necessarily associated with an anterior infarct Arrhythmias may be encountered extrasystoles flutter fibrillation or ventricular tachycardia The tachycardia of flutter or fibrillation may cause a low blood pressure which improves if regular rhythm returns The electrocardiogram (*see* Fig 15 21) shows characteristic changes in the great majority of cases after a few hours in the presence of multiple infarcts the changes are not so typical X ray of the chest may show a normal heart enlargement is associated with severe coronary artery disease or long standing hypertension a ledge or bulge is seen if aneurysmal dilatation occurs

Complications Arrhythmias are frequently met with the commonest being extrasystoles

Heart failure left ventricular failure may induce severe pulmonary congestion and dyspnoea with so much distress that the pain is not mentioned The blood pressure however is lower than usual and this combination should always make one seek the presence of a cardiac infarct It may progress to right ventricular failure or this may be present from the onset.

Rupture of the myocardium may cause sudden death from cardiac tamponade or the interventricular septum may perforate usually inducing left ventricular failure Death may soon follow or the patient may survive for weeks months or years depending on the state of the remaining myocardium

Aneurysmal dilatation of the ventricle follows a large infarct.

Thrombo-embolic phenomena are very frequent and may cause serious deterioration or death when the patient seems to be making a satisfactory recovery Pulmonary thrombi may arise from the leg veins or from the right ventricle if subendocardial damage causes a mural thrombus to form in this chamber Thrombi may also lodge in the brain limb vessels kidneys or spleen from the left ventricle Thrombosis may occur spontaneously in the brain and limbs if arterio sclerosis of the vessels is already present

Painful shoulder frozen shoulder or the shoulder hand syndrome often follows cardiac infarction It may be temporary lasting a few weeks only or lead to permanent disability

Differential Diagnosis Formerly there was a danger that infarction might pass unrecognized As knowledge and fear of the condition increase however symptoms of simple complaints may be mistaken for it and a person s peace of mind destroyed and future life conditioned to needless invalidism

Prolonged angina is almost always due to infarction and this must be excluded in any attack lasting over half an hour

Pulmonary infarction gives rise to shock dyspnoea tachycardia and a fall in blood pressure When pain is present, it is pleuritic in type and the electrocardiographic changes in the standard leads suggest a posterior infarct The chest leads however are characteristic There is rapid respiration and the neck veins are engorged Signs in the lungs and on X ray are not necessarily found for a day or two

Tachycardia due to fibrillation or flutter causes a fall in blood pressure and praecordial discomfort or even pain if coronary artery disease is present Dyspnoea and sometimes heart failure follows if the attack is prolonged The conditions may complicate actual infarction and the exact diagnosis is in doubt until an electrocardiogram is taken or the rapid heart rate controlled

A spontaneous pneumothorax results in chest pain in increasing dyspnoea and if the mediastinum is severely displaced a low blood pressure and rapid pulse and ultimately death Physical examination or a radiogram of the chest elucidate the diagnosis

Pericarditis causes chest pain temperature dyspnoea and leucocytosis An electrocardiogram seen a few days after the onset may even add to the difficulty in diagnosis The S T and T changes are atypical and too widespread and alter over the weeks in a characteristic manner

The pain of hiatus hernia recurs too frequently and is related to posture flatulence and meals There is no shock and the electro-cardiogram remains unchanged The quality and distribution of the pain may cause difficulty A perforated peptic ulcer acute cholecystitis or gall stone colic are less likely to be mistaken for infarction Severe pain from gastric or oesophageal flatulence with radiation to the neck or chest may also be very misleading Dissecting aneurysm causes a severe constant pain usually between the shoulder blades radiating down to the small of the back and may cause vascular and nervous signs and symptoms in the loins and legs The electrocardiogram is unchanged and the blood pressure may be maintained

Prognosis The average length of survival after infarction is 10 years but some live twice as long The younger the age of onset the better the prognosis Pain and shock are no measure of the size of the infarct, and an immediate prognosis is difficult and foolhardy to give The more prolonged and profound the fall in blood pressure the higher and more prolonged the rise in temperature and E S R the worse the prognosis These and the serum transaminase level give some indication of the amount

aVR Lead I aVL

V1 V3 V5 V7

Lead II aVF Lead III

(a)

aVR Lead I aVL

V1 V3 V5 V7

Lead II aVF Lead III

(b)

FIG 15 22 CORONARY THROMBOSIS

(*a*) Healed antero-septal infarct
(*b*) Healed posterior infarct

of myocardial damage Other pointers to a poor prognosis are old age a very large heart the presence of heart failure and history of previous attacks Persistent sinus tachycardia auricular fibrillation ventricular tachycardia and thrombo embolic occurrences are also associated with a higher mortality rate

Treatment When infarction is impending as *when angina rapidly increases the patient should* be rested and kept on anti coagulants Once infarction has occurred pain shock dehydration and heart failure may have to be treated

If the pain is slight A P C or pethidine by mouth may be sufficient to control it In most cases morphia is needed and 15–20 mg (¼ to ⅓ gr) should be given at once intramuscularly If cutaneous vaso constriction is marked it should be given intra venously well diluted If morphia induces or increases vomiting pethidine may be given instead

Shock is treated by rest in the horizontal position and fluids Once it is controlled the patient is sat up in the position in which he feels most comfortable Fluids may have to be given rectally or intravenously if intravenously the rate must be most carefully controlled to avoid the development of pulmonary oedema If severe shock progresses especially if anuria is present attempts to raise the blood pressure by nor adrenaline or metaraminol (Aramine) intravenously are made and digoxin 1 mg may be given if this has not been previously used If cyanosis or pulmonary oedema develop oxygen is given adding to the patient s comfort and helping to relieve pain

Anticoagulants are of proved value in reducing mortality They also seem to increase the formation of anastomotic vessels They are given to moderately or severely ill patients milder cases recovering quite well with general measures only 5 000 units of heparin may be given subcutaneously every 8 hr or 12 500 units of heparin retard intramuscularly *every 12 hr If facilities for prothrombin esti* mation are available this is combined with phenindione (Dindevan) by mouth The older the patient the larger the infarct and the greater the renal or hepatic lesion the smaller the dose needed The usual dose is 100 mg followed by 75 mg 12 hourly regulating the dose by the prothrombin levels In some cases much smaller doses and less frequently larger doses must be given If over dosage has occurred intravenous synthetic vitamin K.I is given slowly intravenously 50 mg in 1 ml if bleeding is occurring If the prothrombin level has fallen too low without bleeding 10 mg may be given by mouth After 4 weeks on phenindione it is slowly withdrawn sudden cessation occasionally seeming to precipitate fresh infarction If infarction has recurred soon after a previous *attack the patient may be kept on an anti-coagulant* for months or years when it may be combined with long acting vaso dilators Quinidine or procaine amide are given if frequent extra systoles occur as these occasionally develop into ventricular tachycardia One of them may be given routinely for the first few days Digitalis is not given routinely if however heart failure develops it is given in the usual way

Rest in bed is continued for at least three weeks, even in slight cases In more severe cases it is continued for four to six weeks or longer if strength is regained slowly or failure is present In slight cases patients are encouraged to move their legs in bed they are helped to the commode and feed and wash themselves. They sit out of bed after 4 weeks and walk about the room in the next week Two to 3 months convalescence are needed before starting work Progress is correspondingly slower in more severe conditions but they may use a commode once they have recovered from shock

Diet in the first few days should consist of fruit drinks only after this it should be expanded to a 1 200 to 1 500 calories diet, unless the patient is obese when weight is lost by giving an 800 to 1 000 calories diet A low fat diet with little roughage is given avoiding flatulence Constipation should be controlled by liquid paraffin combined if necessary with cascara or milk of magnesia Alcohol supplies calories helps sleep and may dilate the coronary arteries it is allowed in moderation if the patient wishes it Smoking should be avoided but if the *patient is a heavy smoker a cigarette after meals* is permitted

During the rest in bed the patient is encouraged by being told that he will return to a normal existence at possibly a slower rate of work This is most important occasionally he loses all confidence and despite a good recovery will not permit himself to perform even the lightest effort in case he harms his heart

CONGENITAL HEART DISEASE

This is an uncommon cause of heart disease forming about 2 per cent of all cases In most cases its cause is uncertain A small proportion is due to *infection of the mother* by German measles in the first two months of pregnancy the development of the heart taking place between the third and seventh week of foetal life Less frequently defects are familial but the majority occur without obvious

cause They result from lack of development or *defective development of the heart or great vessels* or from persistence of vessels which normally atrophy during development or at birth They are *associated with other congenital* abnormalities in a small proportion of cases especially when due to maternal infection they are frequently found with arachnodactyly *and less frequently with* Mongolism They are found in a high proportion of abortions When severe survival after birth is impossible *Especially among the cyanotic group early* death is frequent so that congenital heart disease becomes increasingly uncommon in the higher age groups *Some conditions however such as patent* ductus arteriosus are compatible with survival to old age

Common conditions only or those for which treatment may be attempted will be dealt with

Atrial Septal Defect

The communication between the two auricles may be situated at the antero inferior edge of the incomplete septum primum or at its posterior superior aspect the septum secundum not developing to cover the aperture A persistent foramen ovale is found in about 20 per cent of normal adults causing no symptoms but in rare cases allowing the occurrence of a paradoxical embolism

Mechanism Normally the left auricular pressure *is slightly higher than that of the right side* the larger the aperture however in atrial septal defect the nearer the two pressures approximate The right *ventricle distends more than the left at the same* diastolic filling pressure so that most of the mixed blood is received into that side This may amount to four or five times that going to the left side The right auricle and ventricle and pulmonary artery enlarge as a consequence In some cases pulmonary hypertension is present With pulmonary artery enlargement regurgitation *follows* and *later* right heart failure with or without tricuspid regurgitation With right ventricular inefficiency the blood flow *to the lungs decreases and the pressure in the right* ventricle and auricle at the end of diastole rises leading to a reversal of shunt and systemic cyanosis *This is a late development the cyanose* tardive The left ventricle is poorly developed and the aorta small

Clinical Picture If the aperture is small no symptoms occur the patient living to a ripe old age In others pulmonary infections and paroxysmal tachycardia are met and in the later stages auricular fibrillation may develop Growth may be slow the physique slight and puberty delayed Pregnancy and labour as a rule are borne well In the later stages cyanosis develops heart failure follows soon after Clubbing is *not* common and a late finding The average age at d ath is 40 years

Bulging of the chest wall is present if cardiac enlargement takes place in early life A pulmonary ejection systolic murmur is usually pr sent with a thrill if there is associated pulmonary stenosis A pulmonary regurgitant diastolic murmur (Graham Steell murmur) may develop later Both these murmurs diminish in intensity as right ventricular failure takes place and as the shunt reverses The *pulmonary second sound is split the splitting not* varying with respiration The blood pressure is low and the pulse small *The electrocardiogram frequently shows incomplete right bundle* bran h block Fluoroscopy demonstrates the right auricular and ventricular enlargement the pulmonary artery *may be aneurysmal* and *it* and *its main* branches show a marked pulsation

Lutembacher s Syndrome This is a combination of atrial septal defect and mitral stenosis A mitral systolic and diastolic murmur are heard and the left auricle is also enlarged

Treatment Medical measures consist of avoidance of infection or if contracted *treatment with* appropriate antibiotics or *chemotherapy*

Various surgical methods of closure ha e b n used successfully When associated *with mitral* stenosis operation on the mitral valve produces marked improvement and is performed first the case being reassessed later

Ventricular Septal Defect

This is a common congenital defect usually situated at the upper part of the interventricular septum The apertures vary in size the smaller ones causing the most florid signs the large ones interfering most with haemodynamics

Clinical Picture There are no symptoms and development proceeds normally Cyanosis and clubbing are absent *unless compli ations occur* Bacterial endocarditis may develop at any time and heart failure may develop as a terminal event. This leads to a *reversal of shunt* and cyanosis

The higher pressure in the left ventricle during systole forces blood through the aperture into the right ventricle The stream impinges on the opposite wall with roughening of the endocardium *This* roughened area or the defect itself may become a nidus for circulating bacteria and the seat of bacterial endocarditis

The shunt causes a loud systolic murmur maximal near the sternum in the third and fourth left intercostal spaces *steadily diminishing* as one moves from this area It can also be heard between the scapulae A systolic thrill is present in some cases. The increased *right ventricular stroke volume* may

cause dilatation of the pulmonary artery and regurgitation The increased volume of blood returns to the left side of the heart causing a mid diastolic murmur as it passes through the mitral valve If the defect is small the peripheral pulse is normal if large the pulse is small despite a heaving apex beat and an enlarged left ventricle

The electrocardiogram is usually normal a congenital heart block is rarely found X ray may show a normal heart or enlargement of the left ventricle with pulmonary engorgement

Differential Diagnosis A loud systolic murmur at the base of the heart may be mistaken for aortic or pulmonary stenosis associated with mitral disease if an apical diastolic murmur is present In conjunction with the electrocardiographic and radioscopic findings it may lead to the diagnosis of patent ductus arteriosus

Treatment In most cases the patient leads a normal life care being taken during chest infection or tooth extraction that adequate antibiotic cover is given to prevent bacterial endocarditis Open heart operations now permit the repair of this condition

Patent Ductus Arteriosus

In foetal life blood from the right ventricle passes by the ductus arteriosus to the aorta just beyond the origin of the left subclavian artery At birth the lungs dilate and the blood from the right ventricle passes to the vascular bed of the pulmonary circulation The ductus arteriosus normally closes in the first few weeks of extra uterine life About 10 per cent of congenital cardiac abnormalities consist of persistent patency of the ductus arteriosus usually as the sole finding It is much more frequent in females The pressure being higher in the aorta blood passes from this vessel into the left branch of the pulmonary artery The arterio venous shunt lowers the diastolic pressure It is also lowered by reflexes from the aorta The effect is increased in exercise when the pulse pressure is increased by a simultaneous rise in systolic pressure The volume of the shunt varies depending on the size of the ductus and the pressure gradient from the aorta to the left pulmonary artery With heart failure the aortic pressure falls and the shunt may be reversed with cyanosis Infrequently there is a steady rise in pulmonary artery pressure again with reversal of flow quite apart from heart failure

Clinical Picture There are no symptoms unless failure or infection occurs The gross physical signs may be found early and the resulting solicitude examinations and investigations may result in a marked anxiety state Development is normal unless the shunt is large when retardation of growth may occur The heart size is usually normal but some hypertrophy of the left ventricle may be present The characteristic finding is the so called machinery murmur of Gibson This is a rough murmur which waxes and wanes continuously beginning in late systole increasing into the beginning of diastole and waning before the next systole Its intensity varies inversely with the size of the ductus and directly as the pressure gradient from the aorta to the pulmonary artery It is best heard near the sternum in the second left intercostal space In half the cases there is an associated thrill In children the murmur may be systolic becoming more characteristic as the child grows older The increased blood flow to the pulmonary vessels causes them to dilate and their pulsation may be seen on radioscopy The *pulmonary second sound is increased in intensity* and split Occasionally pulmonary incompetence follows The increased flow to the left heart may cause left ventricular hypertrophy and if the shunt is very large a mitral mid diastolic murmur may be present The electrocardiogram is usually normal sometimes left ventricular preponderance is seen If associated with other abnormalities especially pulmonary stenosis right ventricular preponderance is seen

Differential Diagnosis In children a venous hum may be mistaken for the continuous Gibson murmur This alters with tension of the neck and with the position of the body In aortic and mitral lesions the site and timing of the murmur electrocardiography and radioscopy should make the diagnosis clear Other congenital lesions especially a communication between the aorta and pulmonary artery or a rupture of a sinus of Valsalva into the right ventricle may be differentiated only by catheterization

Prognosis The average age at death is roughly 40 years Some patients live to well over 60 however others with large ductuses die quite early of recurrent chest infections or heart failure and bacterial endocarditis may occur at any time

Treatment If found in infancy and the general condition is good no surgical treatment should be undertaken until the patient is at least 6 years old the best time for operation being between 6–12 years Lung infections should be treated early and vigorously Local septic conditions *e g* infected teeth should be removed under antibiotic cover Any illness or infection not responding rapidly to the appropriate treatment should be investigated to exclude the presence of infective endocarditis

Coarctation of the Aorta

This is a constriction of the aorta just below the origin of the left subclavian artery where the ductus

arteriosus joins the aorta the ductus is closed as a rule The heart itself is usually normal but there may be aortic stenosis or a bicuspid aortic valve with regurgitation The blood reaches the distal part of the aorta by anastomoses between its branches and those arising from the first part and arch of the aorta

Aetiology The cause is unknown it occurs quite frequently and is most commonly found in men The average age at death is 35 years but cases *may live without discomfort into old age* There may be associated dilatation of the first part of the aorta and congenital aneurysms of the cerebral vessels

Clinical Picture The patient is usually free of symptoms until heart failure develops as a result of hypertension He may complain of throbbing in the head or headaches there may be weakness of the legs on effort with or without intermittent claudication due to the diminished blood supply The legs are cold compared to the hands The anas tomotic vessels may be seen and felt coursing under the skin about the scapulae especially when the patient bends forward Murmurs are audible over them and along the course of the internal mam mary artery The heart itself is normal and enlarges *only* when failure develops The blood pressure may not be appreciably raised in childhood but steadily increases as age advances The femoral pulse is *poor and delayed in time this sign should always* be looked for in every case of hypertension The vessels in the feet may not be felt pulsating at all *The renal function is normal* being protected by the *coarctation from the hypertension The electrocar* diogram is normal but develops left ventricular pre ponderance as the blood pressure rises X ray shows a normal heart until the left ventricle increases in *size rib notching due to enlarged intercostal arteries* may be evident at as early as six years

Complications Heart failure is common Rupture of the aorta or a cerebral vessel *may occur* Bac*terial endocarditis* at the site of *constriction or at* anomalous aortic valves may take place at any time

Treatment In the past treatment consisted in the avoidance of sudden or prolonged strain and the *control of infection The narrowed segment* may now be removed surgically the ends being anastomosed or a graft being inserted if the anas tomoses causes undue tension at the junction

Tetralogy of Fallot

This is the commonest form of cyanotic con genital heart disease The tetralogy consists of (1) *hypertrophy of the right ventricle* and (2) stenosis of the pulmonary valve or infundibulum with (3) dextro position of *the aorta* so that it over rides (4) the *high interventricular septal defect* The aorta receives blood from the left and right ventricles the *proportion deciding the degree of cyanosis* In in fancy the ductus arteriosus is still patent allowing some blood to return to the heart for oxygenation, and cyanosis may be absent except during feeding *emotion* or *effort* If the condition is severe death *occurs early after closure of the ductus* but this may be delayed for a few years If the condition is not so severe life may continue into adult life despite continuous cyanosis and dyspnoea on effort

Clinical Picture Nutrition is poor growth is slow and puberty delayed Dyspnoea on effort is usual in extreme cases the patient is unable to cross the ward When dyspnoea occurs patients tend to squat down on their haunches

Cyanosis is present and increases rapidly with any effort The increased venous return to the right ventricle adds to the venous blood entering the aorta from this chamber A compensatory polycy thaemia is present which also adds to the cyanosis Clubbing of the extremities occurs at an early age and may be severe The heart is not enlarged The aortic second sound is accentuated Due to the dextra position of the aorta however this sound *may be very well heard to the left of the sternum* The pulmonary second sound is weak and may be inaudible There is a systolic *murmur over the pul monary area* and in some cases a thrill is felt, due to the pulmonary stenosis

The electrocardiogram shows a *marked right axis* deviation The X ray shows enlargement of the right ventricle the pulmonary outflow tract is *very small* and consequently a concavity results between the aortic knuckle and the left ventricle at the left border of the heart This gives the *typical coeur en sabot appearance to the heart The pulmonary* vessels are small and the vascular lung markings poor

Complications Bacterial endocarditis should be *kept in mind* Due to the polycythaemia vascular thromboses are possible *Haemo-concentration* should be avoided by a high fluid intake if this is likely to occur as in high fever

Treatment *Mild cases* live into adult life and avoidance of infection or excessive *effort* is all that is necessary In more severe cases an artificial ductus is made by anastomosing the subclavian or innominate artery to the pulmonary artery on one or both sides (Blalock Taussig operation) or the aorta to the left pulmonary artery (*Potts operation*) These *manoeuvres introduce blood* which has by passed the lungs into the pulmonary circulation and so increased its oxygenation *Open heart operations* now permit extensive repair of the *interventricular*

septal defect and the stenosed pulmonary infundibulum

Eisenmenger Complex

This consists of a defect of the interventricular septum with an overriding aorta together with enlargement of the pulmonary artery and right ventricle The condition is rare and difficult to diagnose precisely Death does not usually occur till adult life is attained symptoms may be few and late in development

Treatment. Repair of the defects has been attempted by open heart surgery

DISEASES OF HEART MEMBRANES AND MUSCLE

Pericarditis

Pericarditis may occur as a result of local infection or as part of a more generalized systemic affection Either visceral or parietal surfaces may be involved or both together and the inflammation may be localized or generalized

Pathology Pericardial inflammation results in a fibrinous exudate which may become sero fibrinous serous purulent or haemorrhagic Haemorrhagic effusion is due to malignant disease or to tuberculous infection Clinically the pericarditis may be dry or with effusion It may resolve or develop into chronic adhesive pericarditis or constrictive pericarditis These two latter conditions will be discussed separately

Aetiology This may be rheumatic tuberculous bacterial or be due to non specific pericarditis It may be associated with uraemia or cardiac infarction Less common causes are malignant disease periarteritis nodosa lupus erythematosus trauma gumma or parasitic disease Hydropericardium is not necessarily inflammatory and is usually a transudate

Clinical Picture When the aetiology is not inflammatory pericarditis may be quite silent and unsuspected if no effusion develops Should effusion occur symptoms may be produced by its size and by cardiac tamponade Evidence of the cause of the pericarditis such as neoplasm of lung or uraemia will also be found

In acute infective conditions pain occurs only in about 50 per cent of cases and this is usually due to involvement of the adjacent pleura and so is often referred to the distribution of the phrenic and lower thoracic nerves It is sharp and cutting in quality and may be produced by coughing or pressure on the chest wall A dull praecordial discomfort or ache is produced by distension of the pericardial sac in the presence of large effusions

When effusion develops dyspnoea results the patient sitting well up and often leaning forward for relief When the effusion is very large the lungs are best able to expand in this position Compression of other structures *e g* the trachea bronchi and oesophagus may cause cough hoarseness or dysphagia An acute purulent pericarditis will be accompanied by the usual symptoms and signs of intense toxaemia which is part of the original infection and may direct attention away from the heart

The characteristic physical sign is a friction rub This is superficial crunching scratching or leathery in quality and may be increased by pressure with the stethoscope It has a to and fro rhythm or a triple rhythm and follows the heart sounds slightly in time overlapping them It may be fleeting or last for days or weeks and is best heard to the left of the sternum nearer the base of the heart It does not necessarily disappear as an effusion develops

As effusion develops the area of cardiac dullness to percussion widens and the apex beat if still palpable lies within its outer border On lying down the border of cardiac dullness in the second and third left intercostal spaces moves to the left The apex beat disappears and the heart sounds become more distant With large effusions signs of collapse are found at the left base due to compression of the lung (Ewart s sign) Some increase in dullness to the right of the sternum may be found in the lower intercostal spaces

Cardiac tamponade occurs when the intrapericardial pressure interferes with cardiac filling A small rapidly increasing effusion of as little as 500 ml may produce this effect whereas a large collection of a litre or more slowly developing in tuberculous pericarditis may not do so The stroke volume and minute volume fall the venous pressure rises and tachycardia is present The blood pressure falls but is maintained by peripheral vaso-constriction Pulsus paradoxus occurs and the radial pulse may disappear entirely during inspiration Eventually right heart failure develops

Radiology As effusion develops the outline of the normal heart chambers is lost and both borders become convex outwards the heart becomes widened and pear shaped On lying down widening at the base is increased The tachycardia and poor filling with a large effusion result in small wave like contractions on screening Rapid increase or decrease in size and alterations in shape are characteristic

Electrocardiography Early changes consist in elevation of the RS T segment in all leads followed by inversion and flattening of T in the later stages

The voltage of the complexes is decreased The curves may revert to normal on recovery

Differential Diagnosis An enlarged heart with poor contractions and congestive failure may follow hypertension or other causes of left ventricular failure Myocardial infarction may cause pain fever leucocytosis a pericardial rub and electro cardiographic changes making distinction difficult Aortic regurgitation and stenosis with heart enlargement and murmurs may simulate pericarditis Pulmonary embolism with poor heart sounds low output and blood pressure and raised jugular venous pressure also simulates it

Prognosis This depends upon the aetiology

Treatment This depends upon the aetiology When cardiac tamponade occurs, paracentesis becomes necessary This is also done for diagnostic or aetiological purposes Aspiration is performed 1–2 cm inside the left border of the heart determined by percussion in the fourth or fifth intercostal spaces It may be done close to the sternum in the fourth intercostal space on the right or left side or through the diaphragm in the angle between the xiphisternum and the left costal margin close up to the cartilage If pus is present aspiration and antibiotics are tried first but surgical evacuation and drainage may become necessary

Aetiological Types of Pericarditis

Rheumatic Pericarditis

This is still the commonest cause It may be dry localized and evanescent or generalized and accompanied by a serous effusion However large the effusion may be it usually absorbs completely without serious consequences The gravity of the patient s general condition is related more to the associated myocarditis and endocarditis It usually requires no specific treatment

Tuberculous Pericarditis

This is not common infection occuring by direct extension or local lymphatic spread septicaemia or for no obvious cause It may occur at all ages is commoner in males and negroes are specially prone to it Symptoms may be negligible constrictive pericarditis developing before the original condition is recognized It may present as a mild toxaemia a mild pyrexia of unknown origin or as a fulminating disease in tuberculous septicaemia A very large effusion may be present—over a litre—without any symptoms or a dull pericardial ache may develop with symptoms and signs of cardiac tamponade The fluid is frequently bloodstained this may be absorbed or become organized with extreme thickening of the pericardial coverings and the production of a constrictive pericarditis Pleural effusions may also be present Diagnosis is proved by aspiration of the effusion and finding the bacilli in the centrifugal deposit or by inoculation of the fluid into a guinea pig Formerly the prognosis was grave about 80 per cent of cases dying in about 3 to 6 months Now isoniazid and streptomycin have revolutionized the situation the mortality being 10 per cent If the fluid increases to dangerous amounts aspiration is performed to obtain relief If constrictive pericarditis develops surgical relief is necessary whether in the acute or chronic stage

Bacterial Pericarditis

This used to be very common following pneumonia empyema mediastinitis a subphrenic abscess septicaemic states or direct trauma. Mortality was very high despite all treatment, until the introduction of the antibiotics when the incidence diminished and prognosis improved Its presence was often obscured by the severity of the causative condition

Acute Non specific Pericarditis

This is being recognized with greater frequency as the condition is becoming more widely known It may be mild or severe with precordial pain malaise dyspnoea and fever A friction rub is usually heard which may last a few hours only or be present for days A pericardial effusion may develop which is sterile and absorbs without complications It may follow a respiratory infection a specific viral infection such as glandular fever or be part of an allergic reaction Where no preceding factor is found it may be termed acute or non specific pericarditis Treatment consists in bed rest until all activity has subsided Aspiration of fluid may be necessary Antibiotics have not been proved of any use The condition may recur but constrictive pericarditis has not been known to result

Myocardial infarction reaching the outer surface of the heart is accompanied by an overlying fibrinous pericarditis A rub may be heard which may be very fleeting Fluid rarely forms which may be haemorrhagic

Uraemia may be accompanied by pericarditis usually dry It occurs in advanced cases and death usually follows in a few weeks

Neoplasms especially of the bronchi may invade the pericardium with the production of pericardial effusions and tamponade

Polyarteritis nodosa and lupus erythematosus may cause pericarditis with the characteristic signs and symptoms

Although not inflammatory pericardial effusions form in such varied conditions as myxoedema con

gestive heart failure beri beri and xanthomatosis and cholesterolaemia

Adherent Pericardium

As its name indicates adhesions are present between the parietal and visceral layers of the pericardium It is found at between 1 and 2 per cent of autopsies and is usually quite unsuspected during life It varies in degree from filmy strands to strong organized adhesions but these in no way interfere with the heart s function The heart size is normal unless other cause of enlargement is present More intense inflammation may result in adhesions between the pericardium and the mediastinal structures and diaphragm Clinically this produces indrawing of the lower left ribs posteriorly (Broadbent s sign) Numerous other physical signs of these states have been described on insufficient evidence They may be produced by any of the causes of acute pericarditis described in the last section

Constrictive Pericarditis

This occurs in the younger age groups and more commonly in males It may be the end result of an acute pericarditis frequently tuberculous less often pyogenic Sometimes however the onset is insidious and no definite cause is discovered It does not follow rheumatic fever Avascular fibrous tissue continues to be formed until an extremely thick inelastic sac encases the heart which is usually itself unscathed It may be over 2 cm thick adding over 4 cm to the apparent diameter of the heart The fibrous tissue becomes hyalinized and often calcified this varying in extent and thickness

Clinical Picture This depends on the inability of the heart to dilate in diastole The inadequate filling causes a fall in cardiac output and a rise in venous pressure The low output may produce no symptoms at rest and there is no orthopnoea At the slightest effort however dyspnoea results with easy fatiguability The signs it produces are a low blood pressure and pulse pressure and a marked pulsus paradoxus with peripheral vasoconstriction (in an attempt to maintain the blood pressure) The pulse rate rises steeply with effort as this is the only means of increasing the cardiac output The rise in venous pressure causes abdominal enlargement due to enlargement of the liver and ascites This adds to the dyspnoea It also results in engorgement of the neck veins which pulsate very little If not too engorged they are seen to swell in inspiration Generalized dependent oedema follows the ascites and is not usually gross Cyanosis is present due to a slow circulation time Pleural effusions frequently occur especially in the tuberculous cases The heart itself is usually small unless an intracardiac cause is present to produce enlargement It may seem larger than it really is because of the thickness of the pericardial covering There is a palpable diastolic shock and a loud third heart sound due to the high venous filling pressure Atrial fibrillation or flutter is present in 30 per cent of cases Valvular disease is very infrequent Two findings more difficult to explain are an increase in blood volume and a decrease in plasma proteins

Radiology of the heart may be obscured if large pleural effusions are present these may have to be removed for the comfort of the patient when a better view of the heart is obtained There is then seen to be a marked diminution in cardiac movement indeed it may seem to be quite still Calcification is common and may be very extensive and thick (*see* Plates 15 4 and 15 5)

The electrocardiogram shows curves of low voltage with inverted T waves in most leads The P waves may be widened

Differential Diagnosis Congestive failure with a small heart should suggest the diagnosis when the blood pressure and pulse pressure are low and a pulsus paradoxus is present It is to be distinguished from cirrhosis of the liver when the congestion is distal to the hepatic circulation and supporting signs and symptoms are absent In true congestive heart failure oedema occurs before ascites and there is adequate cause in the heart or lungs for the condition

Treatment Active pericardial tuberculosis should be treated by streptomycin and isoniazid usually this results in a regression of the cardiac compression especially if this is mainly due to effusion Once organization has occurred treatment is surgical This is done after adequate bed rest on a salt free high protein diet diuretics and the removal of pleural or pericardial effusions if these do not regress with the above treatment As much of the thickened pericardium as can be removed safely is excised that over the left ventricle is removed first If that over the right ventricle is removed first the increased filling of this chamber may induce acute left ventricular failure the filling of the left ventricle still being hampered by the thickened pericardium Some improvement is instantaneous but further improvement continues for some months

Myocarditis

Previously myocarditis was a common diagnosis without precise diagnostic criteria and included the end result of ischaemic and hypertensive states Lack of precise clinical criteria often led to confusion with neuro circulatory asthenia With more stringent standards and histological control only rheumatic and diphtheritic myocarditis and suppurative myo

carditis were diagnosed with any frequency It is now recognized more frequently both on clinical and electrocardiographic grounds Diagnosis is still difficult as the majority of patients recover without any sequel and even in those who die the micro scopic changes are not specific to any condition

Aetiology Rheumatic fever is the most common and important cause of myocarditis and is associated with endocarditis or pericarditis or both Diphtheria was formerly an important and danger ous cause but is now rarely encountered Myo carditis frequently accompanies sub acute bacterial endocarditis and may produce heart failure or death even when the bacterial infection has been controlled Streptococcal infections as of the throat and tonsils, and pneumococcal meningococcal and gonococcal infections may cause endocardial and pericardial infection as well as a true myocarditis Myocarditis caused by rickettsial and viral infec tions include typhus and scrub typhus influenza poliomyelitis and measles Allergic conditions caus ing myocarditis may follow drugs especially the sulphonamides penicillin serum administration and arsphenamine It is found in acute disseminated lupus erythematosus There remains a group with out evident cause in which death is due to myo cardial failure and there is autopsy evidence of myocarditis—the so called isolated or Feidler s myocarditis

Chronic myocardial changes are found in a wide group of unconnected conditions including sclero derma sarcoidosis Friedreich s ataxia and amy loidosis

Clinical Picture The findings are general local and embolic and are associated with electrocardio graphic and radiological changes General symp toms include those of the original infection—raised temperature tachycardia asthenia and dyspnoea with leucocytosis Palpitations precordial discom fort and extra systoles however may be found without myocarditis being present

Local findings are a disproportionate tachycardia weakness of the first heart sound with a systolic murmur alterations in cardiac sounds a gallop rhythm cardiac enlargement with diffuse apex beat and the development of congestive heart failure The symptoms may be negligible and sudden death may occur in acute infections The blood pressure and pulse pressure fall and cyanosis develops This may be due to peripheral circulatory failure when the veins are collapsed If the low blood pressure is due to myocarditis congestive heart failure fol lows with engorged veins enlarged liver and oedema Both types of failure may occur together Embolic phenomena systemic or pulmonary may occur if the endocardium is also affected Electro cardiographic changes include prolongation of the P R interval varying degrees of heart block elevation or depression of the S T segment, and depression or inversion of the T wave On X ray progressive enlargement of the heart is seen on occasions this may be very rapid

Special Types

Rheumatic Myocarditis

Florid rheumatic fever need not accompany this condition and it may not be found with the acute general condition Fifty per cent of those under 5 years escape and 25 per cent of those under 10 years It is accompanied by endocarditis pericarditis or both and signs of these conditions are evidence of the presence of myocarditis Thus a systolic apical murmur conducted to the axilla may be found and more definitely a soft mid diastolic murmur Both of these may disappear as the patient improves Pericarditis has the same implication The signs and symptoms of myocarditis have already been discussed

Diphtheritic Myocarditis

This has now become very rare in Britain In the first week peripheral vascular failure may occur with signs and symptoms of shock In the second week myocarditis due to the circulating toxins may develop Bradycardia caused by varying degrees of heart block is found but tachycardia usually fol lows in the third week when the block is recovered from Prognosis is serious

Feidler s (Isolated) Myocarditis

This may occur at any age but usually affects young adults males predominating There is no specific predisposing factor in some cases the patient may have had a recent respiratory infection The onset is as a rule insidious with weakness and increasing dyspnoea on the slightest effort Slight substernal oppression palpitations and arrhythmias are found The blood pressure and pulse pressure fall tachycardia and cyanosis develop Heart failure soon follows these signs and the patient succumbs Mural cardiac thrombi may form when pulmonary or systemic embolic phenomena are also present Pericarditis and endocarditis are not present Radi ology may reveal a normal sized heart but it enlarges as the condition advances The electrocardiogram may show little change or those typical of myo carditis in general may be found Death may occur in a few weeks or the patient may survive for several months Diagnosis is by exclusion of the more usual causes of heart failure



Mitral Stenosis



Fusiform Aneurysm of the Thoracic Aorta Showing Generalized Enlargement of the Thoracic Aorta with Aortic Regurgitation and Left Ventricular Hypertrophy

Differential Diagnosis. Peripheral circulatory failure with shock of varying degree and the symptoms and signs of neurocirculatory asthenia such as dyspnoea tachycardia and chest ache with extra systoles may simulate true myocarditis Acute pericarditis cardiac infarction and severe coronary artery disease may also cause mistakes unless carefully excluded

Treatment. This is symptomatic Prognosis depends on the aetiological cause The original cause should be treated with rest until the heart signs and electrocardiographic changes have returned to normal or become stationary If heart failure develops digitalis is used but this is avoided otherwise In diphtheritic heart failure it is best avoided completely

Endocarditis

Bacterial Endocarditis

This denotes an infection of the endocardial surface by bacteria formerly it was subdivided into acute or subacute endocarditis the latter lasting longer than 6 weeks

Incidence The acute cases are caused by pyogenic organisms as a rule the endocarditis being an incident in an overwhelming infection The subacute cases are caused by the streptococcus viridans the enterococcus or *H influenzae* progress is more gradual with intermissions in an inexorable down hill course but the patient may survive for as long as 14 months or more and there are well authenticated cases of recovery Even before the days of antibiotics it was occasionally difficult to subdivide cases on this basis and since their use it is no longer a reasonable means of classification

Aetiology In subacute cases there is always some such predisposing cardiac lesion as a rheumatic valve affection or a congenital defect. The mitral and aortic valves are therefore the most commonly affected The valve lesions are not necessarily severe The condition is rarely implanted on hearts in failure and fibrillation is uncommon Congenital lesions form 10–15 per cent of cases those most frequently found being patent ductus arteriosus interventricular septal defect pulmonary stenosis aortic stenosis and coarctation of the aorta The bacteraemia causing the infection frequently follows tooth extraction tonsillectomy genito urinary operations or an upper respiratory tract infection It may be met with at any age after 5 years and is found in old age It is most common in the second third and fourth decades males predominating slightly

Pathology The bacteria are implanted on the endocardium and become covered by platelet thrombi Later fibrin forms which protects them from the circulating antibodies and acts as a medium for the bacteria The bacteria proliferate more fibrin is deposited and vegetations develop In subacute endocarditis these are fairly firm and the inflammatory reaction in the underlying endocardium is minimal. When emboli break off these do not suppurate With pyogenic bacteria however the reaction is more intense and tissue destruction and ulceration occurs Valves may perforate or chordae tendinae may rupture The emboli usually give rise to abscesses. Myocardial emboli and infection may cause a widespread myocarditis death may result from this despite control of the infection Arterial emboli may cause mycotic aneurysms these follow minute emboli in the vasa vasorum with weakening of the artery wall Any organ may be affected including the lungs when the right heart is involved or a left to right shunt is present. The kidneys are similarly involved but a glomerulonephritis can also develop which may be progressive after the endocarditis is brought under control

Clinical Picture The infective element, the cardiac lesion or the embolic phenomena may dominate the clinical picture but usually all three aspects of the condition contribute their share Fever and tachycardia are always present and in pyogenic cases are both high the general downhill course being extremely rapid In those due to streptococcus viridans the onset and course are insidious with intervals of apparent recovery lasting for weeks so that in the early stages it may be mistaken for recurrent colds or other minor infections Gradually however the patient loses ground he becomes progressively weaker loses weight and develops a moderate or severe anaemia This is associated with a characteristic *cafe-au lait* colour Clubbing of a moderate degree is often present. The spleen is enlarged The white-cell count may be normal or raised but is not usually very high unless accompanying embolic phenomena or with pyogenic organisms The blood sedimentation rate is raised A blood culture should always be done when pyrexia lasting more than a week is present with a rheumatic or congenital cardiac lesion This should be repeated at different times of the day and especially when pyrexia is evident A positive result is usually obtained but a negative result does not exclude the diagnosis if other evidence is strong and treatment should not be delayed in the hope of a positive culture Cultures should be made in different media both aerobically and anaerobically Symptoms of glomerulonephritis may be present the urine contains albumin casts and red cells the blood urea may rise and death in uraemia may occur

A heart lesion is always present except in some cases of overwhelming pyogenic infection A minimal degree of mitral stenosis or aortic regurgitation may be overlooked when diagnosis is made very difficult This is serious in a condition where early recognition makes so much difference to prognosis Changes in murmurs may be due to ulceration of valve flaps rarely new murmurs of a loud, rough character develop suddenly due to perforation of a valve cusp or rupture of a chorda tendinae This is usually associated with a rapid deterioration in the condition of the patient Cardiac deterioration may also be due to a concomitant rheumatic or mycotic carditis This may cause death when the infection has been controlled

Embolic phenomena are numerous the results depending on the position and size of the arteries obstructed Petechiae usually occurring in crops may be seen in the retinae conjunctivae mouth or skin Formerly considered due to minute emboli they are more probably toxic or allergic in origin Under the nails they are seen as linear streaks the splinter haemorrhages of Horder More typically they occur as small very tender swellings on the pulps of fingers and toes on the thenar and hypothenar eminences and the soles of the feet—Osler s nodes They are pink or bluish in colour and last a few days before retrogressing They do not suppurate Larger emboli may lodge in the kidneys with pain in the loin and haematuria (often microscopic) the spleen with pain in the side and an enlarged tender spleen the brain with cerebral phenomena or palsies the eyes with blindness or the limbs with painful cold limbs with or without gangrene Subcutaneous emboli may give rise to quite large swellings Pulmonary emboli are caused by lesions of the right side of the heart A large infected embolus may cause an aneurysm at its site of impact but aneurysms are usually due to minute emboli in the vasa vasorum the weakened wall dilating and occasionally rupturing Depending on its site haemorrhage may be fatal

If recurrences occur they usually become manifest within a month For prevention of permanent cardiac damage and embolic complications it is essential to diagnose and treat these cases early

Differential Diagnosis Recurrent attacks of rheumatic fever give rise to confusion the response to antibiotics the appearance of emboli the enlarged spleen and clubbing help in diagnosis When heart failure is accompanied by fever a blood culture must be taken to exclude the presence of infective endocarditis Emboli may focus attention on any system thus a hemiplegia aphasia sudden blindness or intracranial haemorrhage to the central nervous system recurrent pulmonary consolidation with bloodstained sputum to the lungs haematuria and loin pain to the kidneys and mesenteric emboli and abdominal pain to the gastro intestinal tract. Bacterial endocarditis may be confused with any local or systemic cause of continued pyrexia Thus, tuberculosis malaria typhoid fever systemic lupus erythematosus or polyarteritis nodosa have to be excluded The heart lesion with changing physical signs the continued pyrexia the widespread emboli and petechiae and enlarged spleen and clubbing, will make the diagnosis evident

Prognosis This is now much improved and if treated quickly and adequately the patient is little the worse Ten to twenty per cent still die of heart failure uraemia or cerebral catastrophes Recurrences are less likely to occur in edentulous patients and this should be borne in mind in treatment any dental infection being radically dealt with

Treatment Prophylactic any patients with a known valvular heart lesion should have penicillin before and for 2 days after operations especially those about the mouth nose and bladder

As with so many other infective conditions the advent of the antibiotics has revolutionized the results of treatment If possible the organism is isolated and its specific sensitivity to the various antibiotics determined The streptococcus viridans is as a rule quite sensitive to penicillin and 2 000 000 units per day in divided doses is sufficient but the enterococcus may need very large dosage up to 10 000 000 units a day combined when necessary with probenecid to increase the blood concentration The pyogenic organisms are as a rule easily controlled Treatment is continued for 6 weeks Penicillin may be combined with streptomycin

Rheumatic Endocarditis

This occurs with myocarditis and often with pericarditis Inflammation of the endocardium covering the valve flaps characteristically develops but the lining of the left auricle may be extensively involved Diagnosis depends on the changes of myocarditis (q v) and the development of murmurs A soft systolic murmur may be due to dilatation of the auriculo ventricular ring and may disappear as the patient recovers This also applies to an aortic diastolic murmur A systolic murmur and a mitral mid diastolic murmur however are strongly suspicious of endocarditis Recurrences are common and the valve lesion may increase with each attack The end result may be a severely scarred and contracted valve which so increases the work of the heart that failure ultimately results

CHRONIC VALVULAR HEART DISEASE

Although valvular heart disease has different causes the haemodynamic effects and resulting physical signs are substantially the same so that they may be discussed under common headings Other factors such as hypertension arterio sclerosis carditis and syphilis will affect prognosis but must be considered separately

Aetiology Rheumatic endocarditis is much the commonest cause of chronic valvular affections the mitral valve is most often affected the mitral and aortic combined are next most often implicated the aortic tricuspid and rarely the pulmonary valves may be affected separately or in varying combina tions Syphilis causing aortic regurgitation used to be common but is becoming much more rare Con *genital heart lesions are found in a high proportion* of cardiac patients below the age of 5 years but be come increasingly rare as age advances the affected patients dying Acquired heart disease thus increases in frequency with age Congenital lesions are said to form 1–3 per cent of heart disease in adults

When stenosis is present the proximal heart chamber hypertrophies to overcome the resistance of the narrowed valve orifice With regurgitation both the proximal and the distal chambers are hypertrophied owing to the extra work performed in shunting the regurgitant blood to and fro between them effort wasted as far as the general circulation is concerned

Mitral Valve Disease

This is nearly always due to rheumatic endo carditis though a few cases are congenital in origin The valve ring dilates in the acute inflammatory stage when regurgitation is present Contraction of the organizing inflammatory tissue follows and stenosis becomes increasingly evident There is usually a combination of both states it is un common to find pure regurgitation but tight mitral stenosis with minimal regurgitation is frequently found

Mitral Incompetence

This may be functional the dilatation of the mitral ring being caus d by rheumatic endocarditis failure of the left ventricle or the hyperkinetic states If the original condition is reversible the re gurgitation disappears

Organic mitral incompetence is usually due to rheumatic endocarditis the valve flaps becoming smaller puckered and rigid as the organizing in flammatory tissue contracts The chordae tendinae may also be contracted adding to the difficulty in apposition of the valve edges Much more rarely regurgitation may follow injury to the valves or chordae tendinae by bacterial endocarditis or trauma or to papillary muscles by infarction The effects may then be sudden with rapid deterioration and new physical signs

Mechanism The regurgitation of blood into the left auricle enlarges this chamber With auricular systole more blood is then discharged into the left ventricle which also enlarges and hypertrophies Ventricular contraction returns some blood into the auricle and forces some blood into the aorta The cardiac output is diminished as the force needed to project blood into the aorta is greater than that needed to return it to the auricle The proportions depend on the degree of mitral incompetence The *auricle may enlarge enormously and when it fails* pulmonary engorgement and right heart failure follow Less often the left ventricle fails when de terioration is very rapid

Clinical Picture There may be no symptoms until decompensation occurs Then dyspnoea on effort increases and weakness and easy fatiguability are marked This is followed by signs and symptoms of left and later right heart failure

The pulse is small the blood pressure is low with a small pulse pressure Peripheral vaso constriction is present In the heart the left ventricle enlarges downward and outward with a typical heaving im pulse There is a loud systolic murmur conducted outward to the axilla it may be accompanied by a thrill This is especially so if caused by a ruptured chorda The murmur may be well heard at the angle of the left scapula and the aortic area There is no opening snap but a third heart sound is common The pulmonary second sound is very loud and split Arrhythmias are commonly met with emboli are rare owing to the constant turbulence of the regurgitant blood The left auricle may become aneurysmal when it causes compression of the lung at the right base with impaired percussion note and diminished air entry

Radiology Both the left ventricle and left auricle are enlarged when very large the auricle may be seen to the right of the mid line above the right auricle It is best observed in the right anterior oblique position when it is seen to bulge backward with systole

Electrocardiography Left axis deviation and left ventricular stress are often found and arrhythmias are common

Differential Diagnosis Diagnosis is suggested by an apical murmur This is a frequent finding which may arise within the heart or outside it Exocardial murmurs are due to movement of air with ven

tricular systole in the overlying lung they are soft heard at the apex and vary with position *Innocent* systolic murmurs are frequently found in children and in hyperkinetic states such as anaemia fever and hyperthyroidism They may be quite loud but vary with position and are also heard at the base of the heart Occasionally *very loud rough or high* pitched murmurs are heard at the apex more frequently in the older age *groups in which no* pathology to explain them is found at autopsy it is suggested that they are caused by anomalous chordae tendinae causing abnormal *currents* in the size of the left ventricle have to be taken into account This is increasingly important with advances in cardiac surgery

Mitral Stenosis (Fig 15 23)

This indicates narrowing of the left auriculo-ventricular orifice and is almost always due to rheumatic endocarditis Repeated infections cause progressive fibrosis of the valve margins the valves proper and the chordae tendinae in varying degree the anatomical results depending on the proportional involvement of these structures It usually

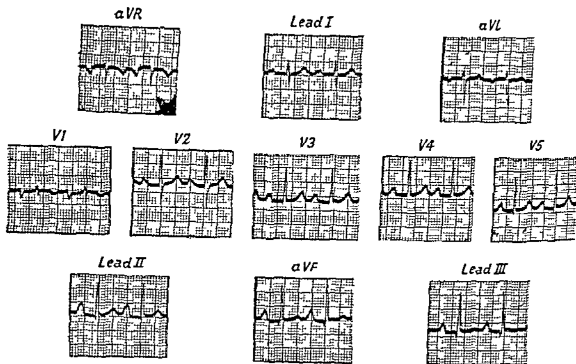


FIG 15 23 MITRAL STENOSIS

Sinus rhythm Right axis deviation Grossly enlarged and deformed P waves

blood stream An apical systolic ejection murmur is frequently found with rigidity or calcification of the aortic valves or dilatation of the aorta due to atheroma It is thus found quite frequently in the elderly and is accompanied by an aortic systolic murmur and ringing second aortic sound As a general rule the louder the apical murmur and the better it is conducted outward the more likely it is to signify mitral disease especially if the heart is at the same time enlarged It is very difficult to decide the relative degrees of stenosis and regurgitation of the mitral valve by the systolic murmur and other factors such as the loudness of the first sound the presence of an opening snap, and the

takes 2 years for clinical stenosis to develop The normal surface area of the mitral valves is 4–6 cm^2 symptoms develop when the area has narrowed to 0 5–1 0 cm^2

Pathological Physiology The normal pressure gradient from left auricle to ventricle is very small, in the region of 1 mm Hg In mitral stenosis this is raised to between 5 and 30 mm Hg the result being that the left auricle hypertrophies and dilates to maintain a normal blood flow It may become aneurysmal holding up to 2 litres Auricular fibrillation is a common complication especially if active rheumatic carditis affects the auricles The left ventricle and aorta remain small The rise in

pressure is transmitted to the lung capillaries and to the right ventricle This is marked in exercise the pulmonary artery pressure rising steeply it may cause acute pulmonary oedema Prolonged capillary pressure rise causes a variable degree of arteriolar constriction and pulmonary hypertension The right ventricle hypertrophies the pulmonary artery dilates and becomes atheromatous and the pulmonary valve may be incompetent. Congestive heart failure follows with occasionally tricuspid incompetence

Clinical Picture Occasionally mitral stenosis is found in old age without any symptoms these are cases which have had rheumatic affections without recurrence the condition of the valve remaining stationary with the heart itself in a well-compensated state Usually however symptoms occur and may be separated into two stages left sided failure and right sided failure

Left sided failure Dyspnoea on effort is marked and orthopnoea soon develops Haemoptysis is frequent It is bright red and short lived when due to a ruptured vessel with pulmonary hypertension and dark red over some days when it follows a pulmonary infarct. Haemoptysis may also arise from varices between the pulmonary and bronchial capillaries in long standing cases Cough due to pulmonary engorgement is frequent especially on lying down at night or on effort. Cough may also be due to attacks of infective bronchitis which are common in patients with mitral stenosis Acute pulmonary oedema does not occur as frequently as in left ventricular failure and is associated with effort emotion or pregnancy Weakness is a common symptom due to the diminished cardiac output Palpitations are common due mainly to nervousness Dysphagia and hoarseness are caused by pressure of the enlarged left auricle on the oesophagus and recurrent laryngeal nerve in advanced cases The enlarged left auricle may even erode the vertebrae with characteristic pain Fibrillation or flutter may develop and precipitate failure They are usually paroxysmal at first but soon become established It is then unwise to try to restore normal rhythm Fibrillation is the more common So long as the rate is controlled at normal levels the circulation is not adversely affected

Right sided heart failure with increasing hypertrophy and dilatation the right ventricle ultimately fails and systemic venous engorgement follows Symptoms of dyspnoea and orthopnoea diminish and the patient feels more comfortable If pulmonary hypertension or pulmonary insufficiency due to recurrent infarction is present however dyspnoea continues unabated It is accompanied by the symptoms and signs described on page 249 Atrial thrombi are more common after failure has occurred these form in both right and left auricles and they may cause pulmonary or systemic complications

Signs. The patient usually has a malar cyanosis cold extremities due to peripheral vaso-constriction a small pulse and a blood pressure and pulse pressure which are rather less than normal. In advanced cases wasting occurs and there are signs of congestive failure The heart is not enlarged the apex beat is tapping in quality and a diastolic or presystolic thrill may be felt there A systolic heave may be seen and felt in the third left intercostal space and also in the epigastrium when the right ventricle is enlarged The first sound at the apex is characteristically short sharp and loud it may be accompanied by a systolic murmur varying in intensity but which may be very loud The second sound is followed by a high pitched loud third sound the opening snap of mitral stenosis which is characteristic of a tight mitral stenosis and pliant valve flaps When the valve flaps are rigid the first sound and the opening snap diminish in intensity This marks the opening of the A V valve and the end of the isometric phase of left ventricular relaxation The mitral diastolic murmur has to follow the opening snap and must be sought at this point in the cardiac cycle It is low pitched rumbling in character and brought out by effort or amyl nitrite the patient lying on the left side There may be a presystolic accentuation of the diastolic murmur if regular rhythm with auricular contractions is present. If fibrillation has developed an early diastolic diminuendo murmur is heard which may disappear before the next first sound The pulmonary second sound is accentuated and split, the second component being the louder A pulmonary diastolic murmur is present if pulmonary incompetence has developed the so-called Graham Steell murmur There may be diastolic shock at the pulmonary area

Radiography The left ventricle and aorta remain small As time goes on the left auricle increases in size and can be seen as a bulge at the left border of the heart (*see* Plate 15 7) The concavity normally present is therefore filled out, and the left border becomes straightened the so called mitralization of the heart shadow The pulmonary outflow tract pulmonary vessels and the right ventricle also enlarge and the transverse diameter of the heart may become very large Mitral calcification may be present

The electrocardiogram shows a widened notched or biphasic P wave with increased voltage Right axis deviation develops and later right ventricular preponderance

Differential Diagnosis A slapping first heart

sound is heard in tachycardias e g Graves s disease A mid diastolic mitral murmur is produced by the rapid passage of a large volume of blood into the left ventricle as in patent ductus arteriosus and interventricular and interauricular septal defects A mid or late mitral diastolic murmur is similarly pro duced in aortic regurgitation usually when well advanced with a large left ventricle the aortic soft diastolic murmur may then be mistaken for a Graham Steell murmur In aortic regurgitation how ever the left ventricle is hypertrophied whereas a true Graham Steell murmur is associated with en largement of the right ventricle A third heart sound at the apex is normally found in young people and may cause difficulty in diagnosis

Treatment Formerly all that could be done was to treat heart failure as it developed The attempt should still be made to prevent deterioration in the general condition of the patient by the avoidance of infections and undue effort But if there is steady deterioration with serious curtailment of effort tolerance or acute left sided heart failure or pul monary oedema occur the patient should be assessed for suitability for surgery Associated coronary artery disease makes subjects over 50–55 years poor risks and even when mitral obstruction is relieved they may progress steadily into failure Surgery is also best avoided in those under 20 years as rheumatism frequently recurs and there is often severe myocardial damage as well Operation should not be attempted in the presence of active rheumatic carditis or when congestive failure cannot be re lieved by medical means Fibrillation or a large heart are not contra indications Bacterial endocarditis should be treated and the patient assessed afresh 4–6 months later When mitral regurgitation or aortic regurgitation are evident operation should be avoided Aortic stenosis when present should be relieved first to operate on the mitral stenosis first may precipitate failure The mitral valve is approached through the left auricular appendage the stenosed valve being split along its line of closure by the surgeon s finger If the adhesions are too firm a special knife is used as complete a split ting as possible being obtained

Aortic Regurgitation

Aetiology This is most commonly due to rheu matic or syphilitic disease It occasionally follows infective endocarditis trauma or a dissecting aneu rysm of the aorta Slight regurgitation without valve defect is met with in hypertension or aortic athe roma

Pathology The thickened contracted and de formed valve flaps are inadequate to close the valve orifice this may be associated with a slight aortic dilatation due to inflammatory softening Later stenosis and calcification may follow The regurgi tant blood increases the work of the left ventricle resulting in dilatation and hypertrophy indeed, it produces some of the largest hearts the so-called "cor bovinum which may weigh up to 1 000 g

Clinical Picture The hypertrophied left ventricle can maintain an adequate circulation even for strenuous activity for many years and the patient may be without symptoms for a normal span of life As a rule the enlarging heart eventually fails especially if hypertension or coronary artery disease also develops concomitantly Left ventricular failure with paroxysmal dyspnoea especially at night and later right ventricular failure then follow A special form of angina may develop especially with syph litic aortic regurgitation the attacks may occur at rest last a considerable time be refractory to vaso dilators and be associated with profuse perspiration Once failure develops the downhill course is very rapid

The essential sign of aortic regurgitation is a diastolic murmur which follows the second sound without pause and is best heard over the aorta along the left border of the sternum or at the apex It is soft high pitched and blowing or breathin in character depending on its intensity It may b extremely difficult to hear and it is best found by listening with the patient sitting forward with the breath held in expiration and the arms held above the head There is often a systolic murmur due to relative stenosis with syphilitic aortitis or actual stenosis with rheumatic valvitis The heart is en larged the heaving apex beat being displaced down ward and outward The aortic incompetence overfills the ventricle causing a strong contra tion and rapid distension of the aorta The latter causes a reflex arteriolar dilatation These facts p oduce characteristic signs—

1 A high systolic and a low diastolic pressure the latter usually being 50 mm Hg or lowe unless aortic stenosis is present. The high pulse pressure causes the arteries to dance"

2 The pulse wave rises steeply and falls pre cipitously the Corrigan pulse

3 The arteriolar dilatation allows capillary pulsation with systole seen in the nail beds the retinae or the skin after producing an erythema

4 A pistol shot sound is heard over the femo al arteries in systole and in diastole a murmur is produced on slight compression beyond th stethoscope

Screening the chest shows the enlarged left ven tricle which is over acting The aorta is somewhat uncoiled with vigorous aortic dynamic pulsation

The electrocardiogram shows progressive left ventricular hypertrophy and stress

Differential Diagnosis. A Graham Steell murmur is similar in character but is associated with pulmonary hypertension most often due to a mitral lesion The right ventricle is enlarged and this produces typical signs and changes in the electrocardiogram With aortic regurgitation the left ventricle is enlarged and the signs in the peripheral arteries are also present Syphilitic regurgitation produces a harsh systolic murmur and a soft diastolic murmur best heard in the 2nd right intercostal space In rheumatic regurgitation the soft diastolic murmur is best heard down the left side of the sternum and at the apex

Treatment This is discussed under Aortic Stenosis

Aortic Stenosis

Formerly considered uncommon it is being recognized with increasing frequency It is divided into non calcific and calcific stenosis the first is almost always due to rheumatic fever and other valves may also be involved The second is usually due to rheumatic affection of the valves but some are degenerative and a few are of congenital origin the other valves are not affected It is more commonly found in males usually over the age of 50 years

Pathology The inflamed valves become adherent at their bases the adhesions extending so that a rigid septum forms A triangular orifice is usually left one quarter or less its original size This septum may become calcified and the calcification may spread to involve the Bundle of His There is usually a degree of regurgitation present The aorta and coronary arteries may be unaffected but with angina in the older age groups coronary atheroma is commonly found

Clinical Picture In well compensated cases there are no symptoms and the condition is compatible with vigorous activity and a normal span of life In advanced cases however weakness dizzy attacks or actual syncope and angina of effort occur Sudden death is not uncommon Syncope is associated with effort the blood supply to the brain becoming inadequate The myocardial ischaemia may result in scattered necrosis or actual massive infarction The left and later the right ventricles may also fail as in aortic regurgitation Fibrillation is uncommon but various degrees of heart block are met with The characteristic sign of aortic stenosis is a loud rough systolic murmur heard best in the aortic area but well conducted to the apex It increases to mid systole then fades disappearing before the second sound It is often accompanied by a thrill the murmur and thrill being conducted to the great vessels in the neck It is best brought out by sitting the patient forward the breath being held in expiration The aortic second sound is weak or absent it may be followed by a diastolic murmur if any degree of regurgitation is present The pulse is late in arriving and prolonged with a slow rise and fall a pulse tracing shows the anacrotic notch on the upstroke of the pulse wave When aortic regurgitation is also present a pulsus bisferiens occurs The blood pressure is normal in compensated cases but as the condition advances the systolic pressure falls and the diastolic pressure may rise In these cases the pressure gradient across the aortic valve rises steadily also and it is here that operation is of value The increased work results in a steady hypertrophy the apex beat moving downwards and outward

The heart may appear normal on radioscopy but left ventricular hypertrophy occurs later Movements of the ventricle and the aorta are small the first part of the aorta may be dilated The aortic valve may be calcified The electrocardiogram shows left ventricular hypertrophy and stress

Diagnosis A rough systolic murmur at the aortic area and apex is frequently found with atheroma of the aortic valve and aorta without stenosis In these cases however the pulse pressure is raised due to the rigid arteries the aortic second sound may be ringing and the pulse full and not delayed

Treatment The treatment of both aortic regurgitation and stenosis used to be that of angina and left and right heart failure when they developed

Valvotomy of the aortic valve may now be attempted when angina or syncope have developed with aortic stenosis results are much worse if heart failure has occurred and the valve is heavily calcified Efforts at replacing incompetent valve flaps or inserting a ball valve in the descending aorta have also had varying degrees of success in aortic regurgitation The ball valve is made of polythene and inserted just beyond the left subclavian artery The blood flow is not impeded and regurgitation is diminished so that the character of the pulses in the lower extremities becomes normal that in the upper extremities remaining that of the Corrigan type Improvement in symptoms and decrease in heart size has followed this operation

Tricuspid Valvular Disease

This occurs more frequently than is generally recognized being demonstrable pathologically in 20–30 per cent of cases of rheumatic heart disease

Other valves are usually more severely affected masking its presence More rarely developmental defects are present Tricuspid incompetence may be functional secondary to failure of the right ventricle

Clinical Picture The patient complains of weakness rather than dyspnoea because the lungs are not engorged unless mitral valve disease is also present There may be evidence of severe congestive failure but the patient remains relatively comfortable and able to lie flat without distress

Tricuspid incompetence is marked by pulsation of the engorged neck veins and of the grossly enlarged liver The heart is enlarged especially to the right there is a loud systolic murmur at the left of the sternum in the fourth space which when very marked may be accompanied by a thrill Cyanosis is intense pleural effusions and ascites are present and later extreme peripheral oedema develops The lung bases may be dry and the pulmonary second sound may be normal On catheterization pressure tracings are characteristic and angio cardiography may demonstrate the regurgitant blood flow If functional these changes clear up as the patient recovers but remain if they are organic

Tricuspid stenosis is usually accompanied by mitral stenosis with which its signs may be confused A rumbling diastolic murmur heard near the sternum increased by inspiration when the pulmonary second sound is not accentuated suggests tricuspid stenosis When the rhythm is regular giant A waves are seen in the neck but usually auricular fibrillation accompanies this condition

Treatment Tricuspid incompetence leads to heart failure and death in about five years Although the patients are more comfortable than those with mitral disease life expectation is less Treatment consists in avoidance of those factors which encourage failure and the treatment of this when it occurs Surgical treatment should be first directed to the mitral stenosis which usually accompanies tricuspid stenosis and this may be enough to make the patient comfortable If necessary the tricuspid stenosis may be relieved surgically later

Pulmonary Valvular Disease

This is rare the least common variety being congenital pulmonary stenosis Rheumatic pulmonary stenosis is very rare and associated with other valve defects Organic pulmonary regurgitation occurs even less frequently due usually to bacterial endocarditis functional regurgitation is more often met with due to pulmonary hypertension (either primary or secondary to mitral valve disease) or to shunts causing increased pulmonary blood flow

Pulmonary Stenosis

This may be isolated or associated with other lesions in particular with interauricular or interventricular septal defects as in the tetralogy of Fallot The stenosis may be valvular or infundibular When it occurs as an isolated lesion there may be no symptoms, even with vigorous activity until the right ventricle hypertrophies and fails Once failure occurs it may progress quite rapidly When associated with interventricular or auricular defects cyanosis develops at first with effort but later as a constant finding Dyspnoea and heart failure develop earlier squatting takes place and clubbing is found

On examination a loud rough systolic murmur is heard at the left 2nd and 3rd interspaces near the sternum it may be accompanied by a thrill The pulmonary second sound may be normal but is usually weak or absent and is then single In advanced cases a diastolic murmur of pulmonary regurgitation also develops It has to be distinguished from aortic lesions or interventricular defects The electrocardiogram shows right ventricular stress in severe cases

Treatment Surgery now offers relief to the mechanical obstruction at the infundibulum or the valve When the right ventricular pressure is higher than 100 mm of Hg operation should be considered

Pulmonary Regurgitation

This is usually functional and due to pulmonary hypertension secondary usually to mitral valve disease chronic pulmonary disease or left to right heart shunts On rare occasions it is secondary to bacterial endocarditis the gonococcus is then frequently the organism found It may be due to rheumatic infection when other valves are always affected

The symptoms are those of the original disease but very soon congestive right heart failure develops

The pulmonary regurgitation causes a diastolic murmur similar to that of aortic regurgitation and heard to the left of the sternum in the 2nd and 3rd intercostal spaces When associated with mitral stenosis this pulmonary regurgitant murmur is known as the Graham Steell murmur

Treatment That of the original affection

PULMONARY HEART DISEASE

Acute pulmonary heart disease or acute Cor Pulmonale is virtually always due to massive pulmonary embolism from a clot in the leg pelvic veins or occasionally elsewhere This is considered on page 382 Chronic pulmonary heart disease ending in failure of the right ventricle may be due to changes in the pulmonary circulation or in the lungs themselves In the great majority it is secondary to lung disease

Pulmonary Hypertension

This is a rare condition and as in a systemic hypertension the cause is unknown in the great majority of cases In about 20 per cent of cases of congenital heart disease with a left to right shunt pulmonary hypertension is found It may be found in some cas s of mitral stenosis and of left ventricular failure but the cause is not clear The cause is more apparent in multiple pulmonary infarcts periarteritis nodosa or bilharzia

Clinical Picture The condition is probably present for a considerable time before symptoms develop but once they occur progress is rapid and death usually takes place in a few months or at most two years Dyspnoea on effort fatiguability and angina of effort develop rapidly followed by congestive heart failure which increases steadily Orthopnoea does not occur The output of the right ventricle falls the circulation slows and peripheral cyanosis is marked The systolic blood pressure is low and the pulse small rapid and regular as a rule Hypertrophy of the right ventricle is shown by a diffuse apex beat strong epigastric pulsation due to the right ventricle and a systolic lift in the 3rd left intercostal space over the pulmonary outflow tract A gallop rhythm may develop over the right ventricle and a pulmonary systolic opening click and systolic murmur may be heard The pulmonary second sound is accentuated and there may be a functional pulmonary incompetence due to dilatation of the pulmonary artery The lung fields are clear in the presence of large venous A waves in the neck a large liver and oedema

The electrocardiogram shows prominent pointed P waves in leads 2 3 and aVF with evidence of marked right ventricular preponderance The X ray shows clear lung fields an enlarged right ventricle and the pulmonary artery and main branches are dilated

Treatment Respiratory function being normal oxygen is of no avail and almost nothing can be done to delay the progress of the condition Tolazoline (Priscol) may be tried as it has been reported that this lowers pulmonary artery pressure When failure develops the usual treatment is given

Heart Disease due to Chronic Lung Infections

The commonest cause of this is emphysema much less commonly it follows widespread fibrotic conditions such as pneumoconiosis bronchiectasis fibrotic tuberculosis post irradiation lung or extensive resection of lung tissue or kyphoscoliosis It is much more common in men than in women the incidence increasing as age advances

Pathology The lung condition leads to incomplete arterial oxygenation which if severe enough results in polycythaemia hypervolaemia and central cyanosis There is an associated diminution in the vascular bed with consequent increased resistance in the lesser circuit and rise in pulmonary arterial pressure This is associated with intimal thickening and narrowing of the arterioles and atheroma in the larger vessels The anoxic tissue state also increases the arterial resistance The pulmonary artery pressures do not as a rule reach those found in primary pulmonary hypertension and the systemic pressure is usually normal The right ventricle may sustain the hypertension and arterial hypoxia for a considerable time before it ultimately fails

Clinical Picture Emphysema usually with increasingly frequent infective episodes with or without bronchial spasm has been present as a rule for years Dyspnoea increases *pari passu* with the emphysema until the patient may hardly be able to walk across a room There may also be central cyanosis varying from a slight sallowness to a black patient this can be brought out by little effort or pulmonary infection These symptoms may be present for years before the right heart enlarges and failure develops once this takes place the course is usually rapidly and inexorably downhill As the condition advances even slight infection may produce heart failure and a fatal outcome With the increased blood volume and increased circulation rate the pulse is full and the extremities warm The systemic blood pressure is usually normal but may be low or high Signs of the lung condition are found Most frequently the heart size is obscured by the emphysema Signs of right heart enlargement are found as with primary pulmonary hypertension There may be an opening click in systole at the pulmonary area and a loud pulmonary systolic murmur the second sound is more widely split and the electrocardiogram may show a partial right bundle branch block The X rays show emphysema the heart may not be enlarged until the condition is

advanced The right ventricle then enlarges lifting the apex and the pulmonary outflow tract and the hilar vessels are enlarged but the peripheral vascular markings are diminished The electrocardiogram shows a high pulmonary P wave and right axis deviation it may show incomplete or complete right bundle branch block or right ventricular stress when the condition is severe

Prognosis The lung condition may be present for years when the right ventricle becomes involved the condition is grave and usually associated coronary artery or hypertensive heart disease is found The progress then is rapidly downhill Recurring bouts of infection or asthma increase the right heart strain and may cause death

Treatment. Emphysema and asthma should be treated by breathing exercises and postural exercises thereby making the best use of what lung tissue is present The slightest lung infection should be treated with the greatest care Once failure has occurred little can be done Oxygen helps the efficiency of the myocardium and diminishes the pulmonary hypertension It may induce confusion and coma due to lack of carbon dioxide but it should be given intermittently and combined with acetazolamide (Diamox) which increases the acidaemia and encourages respiration Sedatives should be given with the greatest care and morphia should be avoided completely When failure is present, digitalis diuretics and a low salt diet are indicated. Venesection is not done the polycythaemia is compensatory and its removal may induce heart failure Carbimazole by diminishing the body's need for oxygen may bring about improvement in some cases

SYPHILITIC HEART DISEASE

Syphilitic heart disease occurs secondarily to syphilitic aortitis primary affection of the heart being extremely rare Fresh cases are becoming increasingly rare Especially since the publicity of the last World War people present themselves much more early and treatment of these early cases is more effective

Pathology The aorta is believed to be invaded via the lymphatics accompanying the vasa vasorum with consequent endarteritis of these vessels This accounts for the site of involvement the lymphatics being most abundant in the first and second parts of the aorta and especially in its first few centimetres From this level the infection spreads upwards and downwards The endarteritis of the vasa vasorum leads to destruction of the media with fibrous replacement and weakening of the aortic wall There is a reactive proliferation of the overlying intima with patches of pearly grey thickening the area between being puckered In most cases calcification is present and atheroma is usually found accompanying the condition It is one tenth as commonly found in the abdominal aorta

Intimal thickening of the sinuses of Valsalva frequently obstructs the coronary ostia Downward spread causes weakness of the aortic ring stretching of the commissures and aortic regurgitation This is added to if the aortic valves themselves are invaded when they become thickened contracted and incompetent Spread to the thoracic aorta may cause a subclinical inflammation with or without dilatation If the process affects the vessel generally a fusiform aneurysm results more usually one part is more affected and dilates before the rest a saccular aneurysm being produced (*see* Plates 15.5 and 15 6) It is much more frequent in males than females It is usually met with between the ages of 35 to 55 but it may occur much later

Clinical Picture Syphilitic involvement of the aorta is frequently found on microscopic examination but is usually without complications and cannot be discovered clinically Slight dilatation of the first part of the aorta causes a relative aortic stenosis with a systolic murmur and a ringing aortic second sound These findings are also present with atheromatous aortic valves and a rigid atheromatous aorta which may be considerably dilated

When aortic regurgitation develops the coronary ostia are usually narrowed This leads to the development of cardiac ischaemia and angina followed by rapid cardiac enlargement and failure often in a few months This helps to distinguish the condition from one of rheumatic origin In this latter angina of effort does not develop unless stenosis of moderate or severe degree is present and failure does not develop for many years unless associated with stenosis Stenosis never occurs in uncomplicated syphilitic aortic regurgitation and the reflux is free The angina of syphilitic aortitis is easily induced and becomes increasingly common at rest until status anginosus occurs The pain is long lasting excruciatingly severe and does not respond in the usual way to vasodilators Sudden death is common but infarction is rare

Fusiform aneurysm of the aorta (*see* Plate 15 8) may be surprisingly symptom free and discovered only on X ray the signs and symptoms of a saccular aneurysm depend on its size and site Very occasionally these may be multiple Unless aortic

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An aneurysm in the first part of the aorta may be associated with aortic regurgitation Symptoms are few though there may be cough and if the ribs are pressed on boring pain in the upper chest. Pulsation may be seen and felt in the 2nd and 1st right intercostal interspaces The aneurysm may erode the ribs and present beneath the skin The swelling is expansile on palpation a systolic murmur is heard and a diastolic shock may be felt over it. Pressure on the right main bronchus or the bronchus to the right upper lobe causes partial or complete collapse of the lung beyond with infection and bronchiectasis The innominate artery may be compressed with unequal pulses due to a lower blood pressure in the right arm rarely unilateral clubbing is also found The superior vena cava may be obstructed usually incompletely with dilated non pulsating veins in the head and neck On radioscopy the swelling of the first part of the aorta is seen to pulsate with systole unless extensive thrombosis has occurred within the aneurysm

An aneurysm of the arch of the aorta may produce a wide range of symptoms even when quite small it may affect any of the important structures passing through the superior mediastinum The trachea may be compressed with stridor cough and phlegm The inflamed adventitia may become attached to the trachea with the production of a tracheal tug This is elicited by pressure upwards on the cricoid cartilage with the breath held Oesophageal pressure causes dysphagia while left recurrent laryngeal nerve pressure produces a hoarse voice and a brassy or bovine non explosive cough The sympathetic chain on the left may be stimulated before the nerves are destroyed so that either a dilated or a contracted pupil may be found the late result is a Horner s syndrome on that side with interference with sweating over the face

An aneurysm of the descending aorta causes great pain of a boring or lancinating quality depending on whether the bodies of the vertebrae or intercostal nerves are affected The non yielding bone of the ribs and centra may disappear entirely leaving the intervertebral discs intact

The distinction between an aneurysm and a solid tumour may be very difficult the best method of making it is arteriography A solid tumour in contact with the aorta may move with systole in a very deceptive manner while an aneurysm may become almost completely solid with laminated clots and not pulsate at all

Complications Rupture of the aneurysm is the most serious and dangerous event An aneurysm of the sinus of Valsalva may rupture into the pericardial sac with rapid death it may burst into the pulmonary artery the results depending on the state of the myocardium An aneurysm may bore its way through the skin or into the oesophagus trachea bronchus or pleura A small ooze of blood may precede a torrential and fatal loss of blood

Heart failure rapidly follows aortic regurgitation and death usually is not delayed longer than a year or so Modern treatment has improved the prognosis of aortic aneurysm and surgery may produce marked improvement in the outlook depending on the site of the dilatation

Treatment. Once syphilitic heart disease has been diagnosed it is best to rest the patient while treatment for the syphilitic infection is begun Therapeutic paradox with diminution in coronary circulation or increase of aortic insufficiency and the possibility of increase in central nervous system affection (if this is also involved) makes rest during the early stage of treatment wise A three week course of potassium iodide and liq hydr perchlor is given first followed by 10 000 000 units of penicillin over ten days given as divided doses of soluble penicillin or daily injections of procaine penicillin This is followed by the usual course of bismuth and arsenic The whole process is repeated in six months time Occasionally three or four such courses are needed to obtain reversion of the Kahn test. Any damage to the heart or coronary arteries is not repaired but the hope of treatment is to prevent progression of the disease Concomitant coronary artery disease especially in the elderly is a *major* factor in determining the results of treatment.

Heart failure and angina are treated in the usual way Aortic aneurysms should be reviewed with a thoracic surgeon

THYROTOXIC HEART DISEASE

Hyperthyroidism

The raised basal metabolic rate in hyperthyroidism necessitates an increased supply of oxygen which is met by an increase in the circulation rate The increased metabolism affects the heart directly increasing its rate of action and it is by this means rather than by a rise in venous pressure that the circulation rate is maintained The muscle and skin vessels are dilated to increase the blood supply and to aid in the heat loss The increased work imposed on the heart as well as its altered metabolism may lead to auricular fibrillation or flutter and heart

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failure This is more likely to occur in the presence of other heart affections such as coronary artery disease or hypertension and so is more often found with increasing age it is very infrequent below the age of 40 years

Clinical Picture Nervousness and tachycardia combine to produce palpitations which may be very distressing Arrhythmias develop and increasingly frequent extrasystoles and paroxysmal flutter or fibrillation precede persistent fibrillation This is found more frequently in older age groups and leads on to congestive cardiac failure In the elderly fibrillation and heart failure may be the first evidence of masked hyperthyroidism usually due to a nodular goitre The heart is over acting with a forceful apex beat in the early stages its size is normal but it enlarges with failure The first sound is short and loud with a systolic murmur most marked at the base The increased circulation rate and peripheral vaso dilatation produces a warm flushed skin a full rapid pulse tending to be collapsing in quality a low diastolic pressure and a resulting high pulse pressure The systolic pressure may also be raised increasing these effects In the young and with regular rhythm failure very rarely if ever occurs

Treatment The cause of the over work being hyperthyroidism treatment is directed to removing this Digitalis has no effect on the tachycardia and very little on the fibrillation Heart failure is treated in the usual way with little hope of improvement until the thyrotoxicosis is controlled

With improvement in the thyrotoxic state the pulse rate falls unless another cardiovascular cause is present to maintain an increased rate Fibrillation may revert to normal spontaneously if not, it usually does so with quinidine The former high circulation rate removes any risk of embolism Rarely fibrillation persists when it can be easily controlled by digitalis

Myxoedema

In common with metabolic changes in other organs the heart is also affected much more often in women than in men Failure does not occur unless coronary artery disease is also present

Clinical Picture There are no specific symptoms of myxoedematous heart disease Heart failure develops with diminishing cardiac reserve Angina is sometimes complained of before failure occurs The pulse rate is below 60/min the cardiac output is diminished and the circulation rate is prolonged The blood pressure is usually lower than normal, but normal or hypertensive levels are frequently found The blood cholesterol is raised to 400–600 mg per cent and the basal metabolic rate lowered to

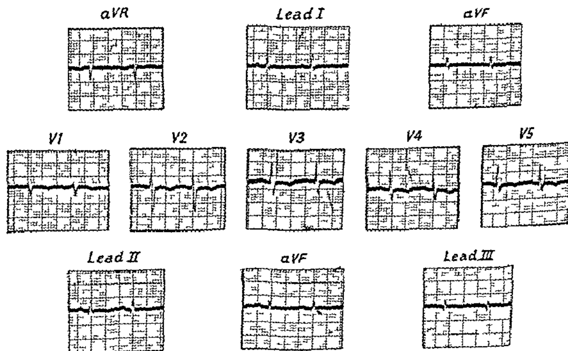


FIG 15 24 MYXOEDEMA

Low voltage curves and inverted T in all leads

-30 to -40 per cent When heart failure develops the pulse rate blood pressure and the basal metabolic rate rise The heart is generally enlarged and there is often a moderate pericardial effusion These changes quickly revert to normal with adequate treatment the heart size then depending on the associated cardiovascular state The electrocardiogram shows a bradycardia with curves of low voltage in all leads (Fig 15 24)

Treatment Once the condition is recognized treatment rapidly brings about improvement. In the presence of failure or angina treatment is started slowly and cautiously otherwise infarction or increased failure may result. In these cases 15 mg (¼ gr) thyroid a day is given for a few days slowly increasing to 60 mg (1 gr) a day over 2–3 weeks Cardiac efficiency improves the pulse rate rises and the electrocardiogram reverts to normal The heart size returns to normal There is usually a definite diuresis with this improvement.

HEART DISEASE AND PREGNANCY

The commonest cardiovascular complication associated with pregnancy is rheumatic heart disease forming over 90 per cent of the cases The other main group is hypertensive heart disease with or without nephritis Congenital heart lesions are much more rare

General Physiological Considerations It has been shown that haemodynamic changes become apparent about the fifth month and gradually increase until just after the eighth month after which they slowly revert to normal about term. They are due to (1) the developing placental circulation which acts as a gradually enlarging arterio venous fistula (2) salt and water retention by the mother with hydraemia and (3) metabolic changes due to the developing foetus and uterus The blood volume rises the heart output per stroke and per minute increases and the haematocrit reading falls The work of the heart increases with these changes until soon after the eighth month and then it gradually decreases until labour begins The increased work is easily borne by a normal heart but results in a fall in cardiac reserve when heart disease is present which may result in serious consequences In labour uterine contractions result in intermittent obliterations of the placental circulation with increasing frequency At delivery it ceases completely The post partum blood loss also diminishes the work of the heart. In the first two days after delivery there is an increase in blood volume A diuresis then occurs and the blood volume returns to normal During these two days heart failure is liable to occur

Rheumatic Heart Disease

The preceding cardiac reserve gives a good idea of how the patient will behave during pregnancy Four grades of disability are recognized The Grade 1 patient is symptom free the Grade 2*a* patient has mild and the Grade 2*b* patient moderate diminution in cardiac reserve the Grade 3 patient has severe symptoms with past or present auricular fibrillation or heart failure Patients in Grade 1 and 2*a* usually go through pregnancy and labour with no difficulty and are none the worse for it. Those in Grade 3 should not be allowed to proceed if discovered early enough Great care is needed in the supervision of those in Grade 2*b* A number enter frank failure but may be improved with adequate treatment and rest so that they have a normal labour safely The earlier in pregnancy that failure develops and the more resistant to treatment it is the worse the prognosis In these matters the family must be considered as a whole A childless couple desperately anxious for a child will take the risk of pregnancy even when failure has already occurred in the past.

Generally the younger the patient, the better the outlook. In older patients the heart condition is more likely to be advanced and obstetric difficulties are more prone to occur The risk is more marked from this aspect in primigravidae

The diagnosis of failure in pregnant women is not easy They became increasingly breathless as pregnancy advances due to the raised diaphragm and increased weight. Their legs may swell due to varicose veins and inferior vena caval obstruction due to the enlarging uterus One must look for venous engorgement in the neck rales at the lung bases and an enlarged liver X ray of the chest will give a clear idea of the degree of pulmonary engorgement.

Congestive heart failure develops slowly but a much more dramatic event is acute pulmonary oedema in mitral stenosis It may occur spontaneously or with pulmonary infection or sudden effort or emotion Its onset is unexpected and it may lead to rapid death If recovered from it may recur at any moment. It is associated with a tight mitral stenosis and the heart may not be much enlarged

Treatment. Once a pregnant woman has been found to have rheumatic heart disease of whatever grade she must be watched with care In all cases

pulmonary infection is treated vigorously and promptly with bed rest until it is controlled Anaemia is treated with the usual iron preparations As breathlessness increases more rest is taken dur ing the day and a careful watch made for the development of signs of failure Once these occur a salt free diet is given and the patient kept at rest in bed with digitalis and if necessary mercurial diuretics If recovery is rapid and complete she may be allowed up but on occasions almost continuous bed rest with digitalis must be continued to term Delivery is usually easy but forceps may have to be applied if the second stage does not advance quickly No benefit is gained by induction of labour after the eighth month or by Caesarean section at term

If heart failure is present in the first three months the pregnancy is best terminated by dilatation and evacuation Failure developing early in the second trimester is best treated by abdominal hysterotomy in some cases however good response to treatment may allow the patient to proceed to term Failure late in pregnancy usually improves well enough for normal labour to occur If failure has occurred in pregnancy sterilization should be performed later Acute pulmonary oedema calls for prompt action. Morphia rest in the upright position oxygen and the rapid removal of 10–20 oz of blood give the best results If she recovers she must be assessed and if necessary valvulotomy performed in the very near future

Hypertension

The patient with essential hypertension of mild degree may be allowed to go to term the kidney function and cardiac condition being carefully watched the whole time The family should be limited to two as hypertension is usually increased by pregnancy and foetal death is common When hypertension is severe pregnancy should be termi nated as soon as possible especially as foetal death is likely otherwise the mother s health may suffer Termination is even more strongly indicated when the hypertension is secondary to chronic nephritis as both increased kidney damage and a dead foetus are usual

CARDIOVASCULAR SYMPTOMS OF PSYCHOGENIC ORIGIN

These symptoms are occasionally grouped as neuro circulatory asthenia (or da Costa s syndrome or cardiac neurosis) They are numerous and may be very misleading They may occur singly or in groups which constitute recognizable syndromes They occur at any age but most frequently in the second third and fourth decades The sex incidence shows a slight female predominance There is in most cases a family history of mental instability or actual illness and a personal history of nervousness social mal adjustment or prolonged ill health in childhood Occasionally single symptoms may occur in well adjusted individuals who have been under considerable stress for a long time Once such symptoms have begun anxiety is increased by the fear of heart disease which increases the symptoms the increased symptoms confirming the patient s worst fears

Clinical Picture Undue dyspnoea on slight effort without evidence of heart disease is characteristic of the condition Close questioning will elucidate any misleading statement that the patient gives in his description Deep sighing respirations at rest occur and these may be mistaken for true dyspnoea by the patient Prolonged deep breathing is not followed by apnoea and breath holding is impaired These phenomena may be explained by increased tone in the muscles of the thoracic cage The sighing is an attempt to relieve the sense of oppression or actual pain most marked in the prae cordium or apical region The discomfort may be felt anywhere in the left chest and may be referred down the left arm It is dragging aching or con stricting in nature and may be relieved by pressure or by a local injection of procaine It may continue for hours or days and may be absent during holi day Another type of pain is stabbing or pricking and this may be very intense always momentary and placed at the apex The region of the apex is often tender Palpitations are frequent and may occur at rest as well as on effort They may develop abruptly but any associated tachycardia is usually of gradual onset accompanying the patient s mounting alarm Tachycardia may be constant or associated with effort if due to effort the return to normal is slow Easy fatigue waking up tired head ache dizziness and sweating of the palms and axillae with cold blue hands are common symp toms The patients are usually tense and anxious and only too willing to admit their fear of heart disease Physical examination of the cardiovascular system electrocardiography and radioscopy may reveal no abnormality On the other hand these symptoms are not uncommonly found in association with organic heart disease and may be related to the patient s anxiety about his condition

Differential Diagnosis The symptoms suggest severe restriction of cardiac reserve but there are

no supporting physical signs The family and environmental background supply positive evidence in support of a psychogenic cause This is most important as the diagnosis is a positive one and cannot be made by the process of exclusion

The condition may be mistaken for thyroid overactivity anaemia subacute rheumatism or prolonged infection such as tuberculosis undulent fever sinusitis or tonsillitis When it is the only symptom left mammary pain may simulate angina very closely but questioning will bring out the fact that there is no constant relationship to effort

Treatment. The history must be listened to with interest and sympathy the social and domestic background being uncovered as far as possible especially as it may bear on the symptomatology A thorough examination is essential and the patient must be reassured that he has no lesion of the heart It will be of help in this if the physician can anticipate or add one or two symptoms thus demonstrating to the patient his knowledge of the complaints This reassures him that the condition is thoroughly understood and helps him to accept the fact that no disease is present If an obvious factor in the patient s circumstances is an exciting cause it should be explained The less obvious and acute the aetiological factor the more important the hereditary predisposition to inadequacy becomes in these cases the prognosis is worse and they should be given psychiatric investigation and treatment In mild cases reassurance and explanation are often sufficient others are helped by graduated group exercises When these symptoms are associated with organic heart disease reassurance may be even more effective than in the absence of such disease The patient will usually have assumed that the symptoms are directly due to his diseased heart and will probably be greatly relieved to hear that this is not so

DISEASES OF PERIPHERAL VESSELS

This term is misleading in that effects may be produced on these vessels by general disease or by lesions which are neither in the vessels nor at the periphery Anaemia or polycythaemia shock or congestive failure drugs and external physical changes can produce symptoms by affecting the peripheral vessels as may a cervical rib cervical spinal arthritis or the shoulder hand syndrome

Diseases of the Arteries

The diseases of arteries are difficult to clarify as their causes are not clearly understood This has resulted in the use of terms which tend to increase the confusion In general however they may be divided into degenerative lesions inflammatory or allergic conditions and vasomotor disorders

Arteries may be affected in their structure or in their function

A degree of arterial spasm is usually found when organic disease is present relief of this gives some indication of the improvement one may expect by medical treatment

The presence of arterial disease may be quite unsuspected for considerable periods It is manifested by symptoms and signs of ischaemia in the part supplied by the artery Acute arterial obstruction may be thrombotic or embolic and is described in surgical textbooks Chronic arterial insufficiency will be described here

Degenerative Arterial Disease

This is the commonest kind of arterial disease and affects all types of arteries

Arteriosclerosis is an omnibus term hallowed by age which includes three degenerative states These are unrelated although they may be found in varying combinations

Atheroma or Atherosclerosis

This is a patchy affection of the intima with secondary changes in the underlying media characteristically affecting the aorta and the larger arteries especially of the lower limb It also affects the medium and small arteries of the heart and brain however and it is this which makes the condition so serious Its incidence increases with age and it is increasingly common after the fourth decade It is much more frequent in men is related to the degree of obesity and is commonly found in diabetic patients and in those with hypercholesterolaemia Hypertension is not a causative factor and is found in its usual incidence at any age A hereditary tendency seems to exist The cause of atheroma is unknown though it seems to be closely related to lipoid metabolism as its incidence is increased in those with hypercholesterolaemia

Pathology Fibrin particles form on the intima which enlarge and become covered by endothelium Fatty changes or fibrosis take place and an atheromatous plaque results In other cases lipoid deposi tions in the deeper layers of the intima are seen which become engulfed by macrophages fresh capillaries develop from the vasa vasorum in the muscular coat and haemorrhage from these enlarges the deposit Central necrosis take place with the formation of an amorphous pultaceous mass

which is shewn on the surface by yellowish streaks which gradually enlarge It may become fibrotic or ulcerate into the lumen with the formation of an atheromatous ulcer Calcification may take place in the mass and extensive plaques of calcareous tissue may form Thrombosis may take place on the ulcer bed or on the damaged endothelium over lying the calcified degenerated tissue The lumen of the large vessels is not encroached upon but this is a serious complication in the smaller arteries of the coronary and cerebral trees

Medial Sclerosis

This is a degeneration of the muscular coat of medium sized arteries most often found in the lower limbs It consists of atrophy of the muscular layer and its replacement by collagenous tissue cal careous deposits and occasionally by actual bone It may be very widespread rings of calcified tissue being felt along the course of the vessel It is found in old age occasionally alone but it is usually associated with diffuse hyperplastic sclerosis It may follow haemorrhage from or thrombosis in the vasa vasorum of the muscular coat The lumen of the vessel is unaffected and the blood supply to the limb unimpaired Dilatation however is impossible so that any increased need as in exercise may not be able to be met This may be responsible for inter mittent claudication The high pulse pressure due to the inelastic state of the arteries results in in creased work of the heart and diminution in the cardiac reserve

Diffuse Hyperplastic Sclerosis (Arteriosclerosis)

This is a response to hypertension and is found in some degree in old age It is widespread but affects in particular the vessels of the kidneys spleen pancreas and the adrenals Hypertrophy and elastosis of the muscular coat take place with hya line thickening of the sub intima and reduplication of the internal elastic lamina When malignant hypertension develops marked intimal thickening takes place either by proliferation or by colla genous deposition as well as the changes already described In severe cases a necrotizing arteriolo sclerosis is found the whole thickness of the vessel wall becomes necrotic and structureless

Clinical Picture Obliterative arteritis of the limbs will be discussed here changes in the cerebral and coronary arteries are considered elsewhere Symptoms rarely occur in the arms the lower limbs being most affected The condition may be present for years without symptoms the arteries on examination being thickened and tortuous or calci fied plaques may be seen on X ray Thrombosis on the atheromatous ulcers in the larger vessels ob structs the lumen and the intimal thickening in the smaller arteries adds to this effect peripherally Ultimately chronic arterial insufficiency develop In some respects progressive coronary artery disease and obliterative arteritis of the limbs are similar Pain on effort may become progressively more severe the course of the complaint being punctuated by attacks of thrombosis with increase in symptoms and possibly death of tissue

Intermittent claudication (*claudio* I limp) is usually the first symptom Pain develops in the foot or calf after walking a certain distance the distance being fairly constant at a fixed rate of progression The pain is aching constricting or cramp like and mounts steadily in intensity as the effort continues It rapidly diminishes and disappears on resting Local tiredness and tenderness continue for a vary ing period afterwards As the condition progresses, pain develops after less and less effort and the after effects last longer The pain never occurs at rest indeed it cannot being produced by an inadequate oxygen supply to contracting muscle It may affect one or both sides Limb pain at rest is due to anoxia of the nerves themselves an ischaemic neuropathy It occurs only in advanced cases when necrosis of skin is imminent or has actually de veloped This pain is intractable to all remedies and is worse at night interfering with sleep and gradu ally leading to attrition of the patient s morale He may gain some relief when the limb is hanging down often he spends his nights with his leg ex posed and in a dependent position

Numbness tingling and stiffness may be found in this condition though they are also characteristic of the intermittent ischaemia of the Raynaud phe nomenon Numbness in obliterative arteriosclerosis is dangerous however slight local traumata may easily lead to gangrene with all its serious conse quences Ulceration and gangrene develop in the late stages of the disease They begin at the tips of the digits and may spread proximally When secondary to trauma they may affect the skin at the heel or elsewhere depending on the site of the injury

Arteriosclerosis usually results in so called dry gangrene with a mummified digit or limb and a thin line of demarcation Thrombo angiitis obliterans and diabetes often cause wet gangrene when the necrotic part is swollen oedematous and infected an area of cellulitis of varying extent spreading centrally The affected limb feels cold depending on the degree of ischaemia This may lead to attempts at warming the limb which may cause actual burns if numbness accompanies the coldness Trophic changes are present in the later stages The skin is dry and shiny the subcutaneous tissue is thin

and atrophic the nails are brittle and the hair falls out and ceases to grow Epidermophytosis is common

Depending on the severity of the condition little may be seen on inspection or atrophic changes ulceration or gangrene are found The skin is usually paler than normal when exposed to room temperature for a time though occasionally it is redder than the other limb and feels warmer due to subcutaneous anastomoses resulting from tissue ischaemia When reflex vaso dilatation takes place however the affected limb is always cooler than its fellow the blood vessels to it being unable to dilate normally On elevating the limb it blanches more rapidly than normal and becomes waxy white in advanced cases On lowering the limb and allowing it to hang down it becomes unduly red and eventually cyanotic the colour changes developing more slowly than normal The veins empty rapidly with the limb elevated and on hanging it down refill in longer than the normal seven seconds With elevation the skin temperature of the affected limb falls more rapidly and to a lower figure than that of its fellow The femoral popliteal posterior tibial and dorsalis pedis pulses are diminished or absent (though as the result of a developmental anomaly the dorsalis pedis pulses of some 10 per cent of normal people are absent) Oscillometric tracings may be taken as a permanent record

Arterial spasm is usually present with occlusive arterial disease and relief of this by reflex vaso dilatation gives a guide to the improvement to be expected from treatment The patient lies horizontally with the limbs exposed until the skin temperature is uniform The trunk is then covered by a heat cradle which is warmed to 45 C the skin temperature in the affected limb rises much less than that of the unaffected limb Sympathetic tone in the arms is much more affected by this method than that in the legs and gives a more precise estimation of vascular spasm In the legs the results may be misleading Spasm may also be relieved by temporary sympathetic nerve block produced by the paravertebral injection of procaine or by injection of procaine near the peripheral nerves themselves This nerve block is more precise in its effect than the heat cradle and gives some guide in the selection of cases for sympathectomy

Radiography demonstrates the presence of calcified plaques along the course of affected arteries and arteriography or aortography will show the precise position of narrowing or blockage of arteries and the course of anastomotic vessels

Treatment. The nature of the condition is explained to the patient and his co operation enlisted Cold must be avoided and the trunk and extremities kept warm Dieting has no effect unless the patient is overweight when he should diet any way Hypercholesterolaemia is found only in a small proportion of cases so that reduction of fat intake need not be advised routinely Anaemia diabetes and heart failure must be controlled when present Alcohol may be beneficial but smoking should be most strongly discouraged The affected limbs must be protected from infection and trauma The feet in particular must be kept clean and a dusting powder used Any fungal infection must be controlled Corns and nails need especial care and the shoes and socks must be well fitting

Vasodilatation is promoted by drugs mechanical methods and by surgical means The effect of drug therapy is by no means certain The methonium compounds pentolinium tartrate (Ansolysen) mecamylamine (Inversine) and Presidal dilate the peripheral vessels by their effects on sympathetic ganglia and so reduce the blood pressure but their hypotensive effects are too intense to allow them to be used as vaso dilators Drugs acting at the vessel wall are tolazoline (Priscol) nicotinyl alcohol (Ronicol) and dibenzyline They are well worth a trial as their effects though variable are in some cases good Other drugs in common use are histamine nicotinic acid papaverine and alcohol Results are variable and as they are often combined with bed rest and other measures difficult to assess In the case of alcohol there is the risk of addiction

Mechanical methods of treatment include postural exercises (Buerger s exercises) and intermittent venous occlusion The patient doing postural exercises first lies horizontally for 3 min The legs are next raised to 45 for 3 min and are then allowed to hang over the side of the bed for 5 min or for 1 min longer than they take to become red in colour The ankles are sometimes moved during this phase The legs are finally rested in the horizontal position for 3 min This cycle of movements is repeated about five times on three occasions during the day Although the results are not definite they seem to improve some cases Intermittent venous occlusion is performed by applying a pneumatic cuff to the thigh and obstructing the venous return but the results are not very satisfactory If the condition is not too severe the patient is instructed to walk each day resting at the point when pain is produced This also encourages the formation of a collateral blood supply

If the response to vasodilator drugs is good and especially if the skin becomes redder and warmer after procaine injection near the lumbar sympathetic ganglia lumbar sympathectomy is indicated provided the condition is advanced enough to warrant it On occasions an arterial obstruction is found in

a position where the segment of the artery may be removed and replaced by an arterial graft When in the aorta iliac or femoral vessels the results may be very good but more distally they are less predictable When ulceration has occurred great gentleness is used when dressing the leg warm soaks of boric acid or Eusol with Varidase if the slough is slow in separating and penicillin systemically are given If healing will not take place if gangrene develops and if pain becomes intractable amputation may be the only adequate course Anticoagulants have been used as a prophylactic when symptoms are increasing The results are variable and have to be weighed against the dangers inherent in this treatment

Dissecting Aneurysm of the Aorta

This is an uncommon condition usually a result of a cystic degeneration of the media of the aorta It is met with in the elderly the incidence is higher in men It may be associated with atheroma hypertension or both Effort seems to precipitate the condition in some cases

Pathology The media of the aorta first degenerates and the aneurysm begins by haemorrhage from a vasa vasorum forming a haematoma As this increases in size the media is split or dissected The blood may rupture into the aorta by an atheromatous ulcer or outwards into the mediastinal abdominal or pericardial cavities When the aneurysm is secondary to effort it may begin by splitting of the intima often at an atheromatous ulcer The degree of medial splitting may be slight or include great lengths of the aorta Pressure on the emerging arteries causes signs and symptoms of vascular obstruction this may affect the lumbar renal or even the iliac vessels On rare occasions the condition is self limiting and healing follows

Clinical Picture The onset is sudden agonizing pain strikes the patient usually in the retrosternal region or between the shoulder blades as the commonest site of origin is the thoracic aorta The pain may spread to the head and neck arms or down the back to the lumbar region or the legs reflecting the spread of the aneurysm as it tears its way through the media If the process affects the origin of the coronary arteries actual infarction and sudden death follow cardiac tamponade by rupture into the pericardium may also occur Unequal pulses in the arms or the legs may be present and arterial insufficiency or even gangrene follow The severe pain of anoxia of the nerves to the arms or legs with loss of motor and sensory activity and absent reflexes may develop Death usually follows in a few hours or the patient may survive for several days or weeks The condition may be confused with cardiac infarction but the electrocardiogram is normal unless pressure on the coronary arteries occurs and the blood pressure does not fall unless shock is very severe

Treatment This consists of morphia and complete rest and antibiotics for any secondary chest infection due to the bed restriction Anticoagulants are avoided

Inflammatory or Allergic Conditions

Thrombo-Angiitis Obliterans (Buerger's Disease)

This is an uncommon affection of peripheral vessels segments of arteries and veins being inflamed leading to thrombosis and ultimate organization with impairment of blood supply to the part beyond

Aetiology Its cause is unknown Infection or an allergic response to various antigens with production of a collagen disease have been suggested but neither has been proved Smoking seems to exacerbate the condition though it may occur in non smokers In some cases patients smoke more than usual because of the pain of the complaint. It may be found in any race or country but preponderates in Jewish people The sex incidence is striking the proportion in some series being 99 males to 1 female When it occurs in females it is usually mild and may be mistaken for Raynaud's disease It is met with at any age between 17 and 70 years but most often between 20 and 45 years

Pathology Thrombo angiitis obliterans is a segmental inflammation affecting all three coats of arteries and veins with thrombus formation The inflammation spreads into the surrounding tissue and involves the adjacent nerves Polymorphonuclear leucocytes and occasional giant cells are seen softening takes place and organization of the inflammatory mass follows the whole being knit into a firm fibrous nodule Recanalization often takes place aiding the anastomotic supply of blood to the more distal part The lesions mainly occur in the deep vessels of the lower limbs but the superficial veins may be affected alone singly or in groups at varying intervals a fleeting or migratory phlebitis The condition is a general one the brain heart abdominal and pulmonary vessels as well as the limb vessels being affected

Clinical Picture In about 20 per cent of cases migratory phlebitis precedes or accompanies disease of more deeply placed arteries Tender red segmental swellings are found along the course of the veins The acute phase of more deeply placed arteritis and the associated neuritis is marked by severe lancinating pain along the course of the affected nerve worse at night Depending on the

size of the affected artery it may or may not be accompanied by evidence of arterial obstruction Raynaud s phenomenon may be present in the inter mediate stages when the vascular spasm may be relieved considerably by sympathectomy In ex tremely rare cases the upper limbs are affected first

The patient usually presents with chronic arterial insufficiency in one or other lower limb This is the late result of several attacks of arteritis in the past the anastomotic vessels gradually becoming inadequate to supply the affected limbs The con dition has usually followed a fluctuating downhill course for several years before this state is reached Intermittent claudication develops the pain occur ring after a precise amount of effort It is felt in the toes feet and calves and is a constant aching pain increasing steadily until the patient is forced to stop relief then rapidly follows As the state of ischaemia increases the onset of pain is earlier and it lasts longer and takes longer to diminish until the patient is almost completely incapacitated The limb becomes colder and paraesthesiae develop these may be the earliest symptoms of developing ischaemia Pain of neuritis occurs at rest and is lancinating in character Ulceration may follow the slightest injury and the ulcers which are extremely painful may enlarge and become infected This ulcer pain is aching and boring constant by day and night and relief is difficult to obtain Gangrene follows usually moist and amputation is then the only means of treatment

On examination the foot is cold and arterial pulsation is usually absent Once symptoms have developed lesser changes are also found in the other limb Nutritional changes are seen The skin is dry and scaling the hair is lost and the nails become brittle and discoloured Trichophyton infection is often found On elevating the leg extreme pallor rapidly develops on lowering it the veins fill very slowly and the leg gradually develops a deep bluish red colour Reflex vaso dilatation tests show definite arterial obstruction with varying degrees of vaso spasm

Prognosis Acute incidents occur with temporary and diminishing improvement until arterial obstruc tion ends in severe claudication and later gangrene The whole course usually takes about 6–12 years but it may be much shorter even as little as 6–12 months or much longer It is usually progressive however and in some cases serious cardiac or cerebral complications occur with corresponding deterioration in the patient s condition

Treatment As thrombo angiitis obliterans is a chronic relapsing disease of widely varying natural history assessing the value of treatment for it is very difficult No remedy has any certain effect on its course and the most that can be said of treatment is that it delays the development of complications or relieves the symptoms The patient is advised to wear warm clothes generally and especially warm gloves and socks with well fitting shoes and to take great care of the skin and nails in the hope of preventing gangrene or injuries that may lead to gangrene He should be strongly urged to stop smoking completely since there is good evidence that tobacco aggravates the process Buerger s exercises or intermittent venous occlusion (*see* page 293) or both carried out three or more times daily probably have some influence in forming and maintaining the collateral circulation Vaso-dilator drugs such as nicotinyl alcohol (Ronicol) tabs 2 t d s or dibenzyline mg 10 t d s may give some symptomatic relief Especially in the acute phases anti coagulant drugs may hinder the development of thromboses Analgesic drugs are usually needed for the pain if this is very severe the appropriate nerve may be injected with alcohol Chemical or surgical sympathectomy is useless in advanced cases but if the condition is worsening or spasm is present it may for a time improve the circulation When infection and ulceration develop systemic and local antibiotics should be given and the lesion kept clean Strong antiseptics should never be used In the end amputation is usually needed for ad vanced ulceration or gangrene

Periarteritis Nodosa

This is a systemic disease affecting the medium and small arteries throughout the body with result ing pleomorphic symptomatology

Aetiology It is an uncommon condition which may occur at any age from a few months to extreme old age but is most commonly met with between the ages of 20–40 years It affects males four times as frequently as females The majority of cases develop without apparent cause but others follow the administration of drugs or foreign proteins and some may be the consequence of various infections The condition then seems to be a sensitivity reac tion and its response to ACTH and cortisone seems to bear this out

Pathology Foci of coagulation necrosis occur throughout the body affecting the medial coat of the medium sized arteries A fibrinoid exudate forms which becomes invaded by polymorpho nuclear leucocytes and giant cells this later be comes organized into fibrous tissue The adventitia is also affected and the intima becomes oedematous with proliferation of its cells Thrombosis of the vessels may result with infarction of the tissue it supplies When only part of the artery wall is affected weakening of this portion results in the

formation of an aneurysm which may rupture the result depending on the artery involved The small inflammatory swellings of the disease process may be seen and felt when they involve skin or muscle

Clinical Picture The manifestations are local and general The condition follows a fluctuating course periods of activity of varying severity and duration alternating with those of complete remission Activity is marked by sweats and fever with on occasions rigors and chills Malaise weakness anorexia weight loss and tachycardia are present The white cell count is raised with eosinophilia in those cases of obvious sensitivity The E S R is also raised In mild cases these changes are naturally correspondingly slight

Local symptoms and signs are legion and may affect any system in the body They are caused by the arterial thrombosis and consequent infarction The vessels of the kidneys alimentary tract heart and central nervous system are most frequently affected Kidney lesions result in painless haematuria albuminuria and urinary casts Renal function becomes increasingly impaired and in some cases uraemia develops Hypertension is usually found as the condition advances this may lead to heart failure or cerebral complications Alimentary symptoms include severe abdominal pain nausea vomiting and diarrhoea Bloody diarrhoea and pain mark the infarction of a mesenteric vessel If vessels of the gut itself are involved ulceration with haemorrhage or perforation develop The vessels of any organ in the abdomen may be involved simulating the presence of appendicitis cholecystitis or pancreatitis In the heart pericarditis is frequent rarely an aneurysm of a superficial artery forms and may rupture with death due to tamponade Multiple interstitial myocardial lesions may lead to fibrosis and gradual heart failure More rarely still a larger artery is affected with more typical features of cardiac infarction Very rarely indeed the endocardial vessels may be involved In the nervous system central lesions may mimic any lesion at any site in the brain The peripheral lesions are often very painful when they affect the sensory branches Lesions of the vessels of the muscles and skin may also be very painful and in the case of the muscle arteries may result in intermittent claudication

Treatment No effective treatment was known until recently symptoms being alleviated as they arose The condition was in almost all cases fatal its duration depending on the frequency and duration of the remissions It may last from a few days to many years ACTH cortisone or prednisone now afford striking relief 15–20 mg of prednisone t d s is given for a week and 10–15 mg t d s for a further 3–6 weeks The dose is then gradually diminished over another 4–6 weeks depending on the severity of the attack In some cases a maintenance dose of 5 mg t d s is continued for months If fresh symptoms appear the drug is re started and continued for a further few months until the condition remains quiescent Before the prednisone has caused diminution in the symptoms analgesics are needed for the pain Damage done by arterial thromboses is permanent and the ultimate outcome will remain in doubt

Temporal Arteritis

This is closely related histologically to periarteritis nodosa but forms such a distinct clinical entity that it is described separately It occurs in elderly people usually over 60 years slightly more frequently in females without preceding cause It is usually self limiting but may produce serious complications before this takes place and in rare instances death may occur from cerebral or coronary thrombosis in a few weeks

Clinical Picture General symptoms precede or accompany the local condition The onset is usually gradual with weakness anorexia fever sweating and weight loss which may be marked The patient is depressed and complains of severe headache and pains in the joints and muscles Anaemia develops the white cell count is raised and the E S R is high Locally the temporal and occipital arteries become inflamed and very tender causing extreme pain This is constant aching or throbbing and exacerbated by chewing or pressure so that the patient cannot wear a hat or rest the head at night Pulsation diminishes and disappears and the vessel is swollen and red and surrounded by an area of cellulitis This gradually resolves in a few weeks leaving a firm non pulsating cord Other vessels affected are the retinal arteries with unilateral or bilateral blindness and the cerebral arteries with serious sequelae due to thrombosis Histological changes are found in the coronary vessels the carotid pulmonary mesenteric renal and iliac arteries Rarely thrombosis is found in the coronary arteries with infarction and those to the lower limbs may be similarly involved

Treatment In the past treatment was unsatisfactory but the disease can now be controlled by ACTH cortisone or prednisone in the same dosage as for periarteritis nodosa Before the prednisone has caused diminution of symptoms analgesics are needed for the pain

Vasomotor Disorders

Raynaud s Phenomenon

This consists of intermittent attacks of coldness and changes in colour of the fingers and toes of

symmetrical distribution which may or may not be associated with necrotic changes in the skin Tingling and throbbing may be present during the phase of recovery

Aetiology Sometimes the aetiology is unknown and the patient is said to have Raynaud s disease or primary or idiopathic Raynaud s phenomenon This variety usually occurs in women between 20–40 years of nervous temperament and asthenic build has a familial tendency and may gradually disappear about middle life In some cases however the attacks become progressively more severe and frequent causing necrosis and loss of the finger tips

Secondary Raynaud s phenomenon may be due to several conditions It may accompany scleroderma Ergot can produce it and it may occur after eating bread tainted with ergot, or after over-dosage of this drug Trauma when using pneumatic drills pounding machines or sometimes crutches may cause it. Conditions of the central nervous system such as causalgia neuritis spina bifida and nervous changes secondary to cervical spondylosis are also possible causes It is occasionally secondary to obstruction of the brachial artery by arteriosclerosis or thrombo angiitis obliterans

Pathology Spasm of the digital vessels and arterioles results in pallor and coldness of the digits The cause of the spasm may be an abnormal response to cold or to over activity of the sympathetic supply to these vessels or to both Experimental evidence is conflicting and all cases cannot be explained on one hypothesis alone Arterial relaxation gradually occurs with a very slow blood flow into the dilated capillaries causing a deep cyanosis of the skin As the arterioles continue to relax the blood supply improves and a warm red digit results accompanied by tingling and throbbing

Large arteries such as the brachial and radial are not affected Only in the advanced stages do the digital arteries show any histological change when intimal thickening and hypertrophy of the muscle coat are seen and thromboses may be present especially if there is skin necrosis Trophic changes in the nails and skin of the affected digits occur with ulceration necrosis and gangrene When associated with scleroderma thickening of the subcutaneous tissue by oedema takes place to be followed by atrophy and contracture pressure on the small vessels interferes with nutrition and the distal phalanx becomes absorbed

Clinical Picture At first the attacks are mild and infrequent, and are precipitated by cold or emotional stress They effect the tips of the fingers only the thumb being usually spared and soon pass off Later they become more easily produced last up to several hours and the condition spreads towards the palm At the onset the affected fingers are dead white and remain so until recovery begins when they become a mottled blue and later a bright red the digits then being warm and throbbing and affected by intense tingling The hands alone are most commonly affected In some cases both hands and feet and rarely the tips of the nose and ears and the cheeks are involved The attacks naturally occur most frequently in winter and may be aborted by warming the hands If the condition is progressive areas of ulceration going on to necrosis are found at the finger tips if scleroderma is present the distal phalanx may be lost.

Diagnosis The colour changes described precipitated by cold or emotion in young adult females characterise Raynaud s disease It is important to look for the causes described under aetiology of secondary Raynaud s phenomenon

Treatment. When Raynaud s phenomenon is secondary the treatment if any is that of the primary condition Otherwise the attacks can to some extent be prevented by keeping the body and the extremities warm in cold weather Smoking is discouraged as it is known that nicotine causes constriction of arteries Vaso-dilator drugs such as tolazoline (Priscol) nicotinyl alcohol (Ronicol) and dibenzyline should be tried in as large doses as the patient can tolerate Sometimes they are of considerable benefit When the condition is progressive these drugs are usually ineffective and removal of the stellate or the lumbar sympathetic ganglia or section of the pre ganglionic fibres should then be carried out The operation improves most cases and gives marked relief in some but its effect tends to wear off in time It does not affect structural changes that have already occurred Even when scleroderma is present the blood supply may be improved though the general progress of this condition is not affected

Erythromalalgia (Erythermalgia)

As its name implies this is a condition of redness and pain in the extremities The term erythermalgia has been suggest d as an alternative because it also implies the sense of heat which is invariably present. It is rare and its cause is unknown It occurs in men and women and although it usually begins in middle or old age it may be found in much younger people

Clinical Picture The onset is gradual Most often the feet alone but sometimes the feet and hands together are affected In the early stages a small area of the extremity is affected but later the whole foot or hand may be involved Attacks begin whenever the temperature of the limb is raised to a critical point and continue until it is cooled Thus

they are induced by warming the body or limb by exercise or by increasing the venous pressure as when the limb is hanging loosely The arteries dilate the blood supply to the part increases and it becomes red hot slightly swollen and painful The pain may be slight at first but increases until it is excruciating Sweating of the part is usual and may be profuse Trophic changes do not occur

Differential Diagnosis Pain and redness are met with in arteriosclerosis but the limb is never hot a very similar condition is also found in polycythaemia Painful warm limbs are also found in peripheral neuritis and in poisoning with heavy metals such as thallium arsenic or lead

Treatment is as a rule unsatisfactory Occasional cases respond dramatically and for considerable periods to acetyl salicylic acid in quite small doses Cooling elevating and keeping the part at rest may abort the attacks When attacks are very easily induced and the pain is distressing section of sensory nerves to the part may become necessary

Acrocyanosis

This is a condition of blueness and coldness of the extremities Its cause is unknown It seems to be a functional derangement of vascular control in which increased tone in the arterioles is combined with a dilatation of the capillary bed and venules It is of symmetrical distribution affecting the arms and hands more often than the legs and feet It most frequently occurs in plump young women when it affects the legs it is known as erythrocyanosis crurum puellarum frigida

Clinical Picture The extremities from above the wrists and ankles to the tips of the digits are a mottled bluish red colour and cold or cool depending on the weather They are usually moist and sweating may be profuse In warm weather the parts become warm and red Slight puffiness of the subcutaneous tissue may be present but there are no trophic changes Some diminution of sensation may be found Chilblains are a common accompaniment The condition continues for months or years

Differential Diagnosis It is distinguished from Raynaud s phenomenon by its persistence and the lack of pallor pain and trophic changes The mottled cyanosis found in dependent parts associated with arteriosclerosis is differentiated by the lack of arterial pulsation in the arteries to the part and possibly by trophic changes

Treatment This is unsatisfactory The symptoms can be diminished by keeping the hands and feet warm but young women cannot easily be persuaded to wear thick woollen stockings Short of this vasodilator drugs (page 293) may be given though their value is uncertain In extreme cases when chilblains are associated and lead to infection sympathectomy may be tried the results in some cases being very good

Diseases of the Veins

Varicose Veins

These may be primary or secondary

Primary varicose veins have a hereditary tendency Otherwise their aetiology is uncertain though mechanical causes such as long hours in the standing position cough constipation and heavy lifting may play a part

Secondary varicose veins follow obstruction of venous return They occur with pregnancy pelvic neoplasms ascites and especially after ilio femoral thrombophlebitis

Varicose veins are very common especially in women over the age of 30 years

Clinical Picture There are often no symptoms. The patient may complain of heaviness and fatigue of the muscles cramps and aching burning or stabbing in the leg though these seem to be due more to her awareness that she has varicose veins than directly to the veins themselves

On examination the veins are lengthened tortuous and dilated the arterial pulses are normal and the leg is warm On elevating the leg the veins empty rapidly Trendelenburg s test consists in thus emptying the veins compressing the internal saphenous vein at the groin and quickly standing the patient On releasing the pressure the vein fills from above in a few seconds If the pressure is maintained dilated communications with deep veins are identified when present

Complications Chronic venous insufficiency may lead to oedema venous stasis varicose eczema a chronic form of cellulitis and varicose ulceration Thrombo phlebitis will be discussed later

Treatment This is aimed at improving the appearance of the legs and in severe cases the prevention of complications It consists in the use of supportive bandages or elastic stockings and sclerosing solutions either alone or with more extensive surgical procedures Details will be found in textbooks of surgery

Thrombophlebitis and Phlebothrombosis

These terms indicate intravenous clotting with partial or complete obstruction to the blood flow Pathological distinction between them is difficult, but clinically they are quite distinct Thrombophlebitis implies a local causative state either traumatic infective or neoplastic local and general effects are usually present Phlebothrombosis implies a spontaneous clotting in the vein due to more

general cause the condition is often silent with little general effect, and its occurrence may be demonstrated by a pulmonary embolism

Aetiology Three factors encourage the formation of an intravenous clot

(1) A local lesion of the vessel wall The introduction of needles or polythene tubes even when aseptic the injection of concentrated solutions and local injury may cause clotting Injury may be quite slight as in axillary vein thrombosis or in some cases in the lower limb Local infection or a neoplastic process also result in thrombophlebitis

(2) Slowing of the blood flow This is the main cause of phlebothrombosis It occurs in patients confined to bed especially if obese or in cardiac failure Tight bandages or pillows beneath the knees add to the risk Obstruction by abdominal masses pelvic neoplasms and pregnancy are other factors

(3) Heightened coagulability of the blood This follows tissue injury and so is found after operation cardiac infarction or delivery when involution is taking place Polycythaemia primary or secondary to haemoconcentration favours clotting Multiple thrombo phlebitis is found in thrombo angiitis and may also be associated with a carcinoma often in the pancreas lung stomach colon or ovary

Pathology Either spontaneously or at a site of local trauma thrombosis occurs usually a white clot forms a mixed clot developing proximally from this This lies free in the lumen of the vein in the case of phlebothrombosis but soon becomes attached due to secondary phlebitis In the case of thrombophlebitis the clot is firmly attached from the start In both cases however extension proximally may occur with the formation of a long clot free in the lumen At this stage it is friable and may give rise to emboli This is very prone to occur when it extends from a smaller vessel into the lumen of a larger vessel the free flow of blood along the large vessel may carry a part of the unattached clot along with it Later the clot becomes organized and attached to the vessel wall

Clinical Picture This depends on the size of the vein its position in the limb and the degree of inflammatory reaction present

Phlebothrombosis causes few symptoms and it is often unsuspected until a pulmonary infarction occurs An increase in the size of the limb due to oedema with local tenderness on pressure is found on examination Dorsiflexion of the foot may cause pain (Homan s sign) but it is not a reliable test. Slight temperature and tachycardia may be noted

Thrombophlebitis is accompanied by local pain which may be slight moderate or severe and redness and tenderness along the course of the vein Venous obstruction results in oedema varying in extent according to the site of the lesion The leg may be of normal colour and temperature or when there is ilio femoral thrombosis it may be mottled cyanosed and cold due to reflex arterial spasm General symptoms of malaise fever tachycardia and leucocytosis accompany these local effects In general pulmonary emboli are less frequent unless proximal extension has occurred

Complications. The most important is pulmonary embolism The emboli may be small or large single or multiple (*see* page 382) Permanent venous insufficiency may occur with a permanently enlarged leg which may be a serious handicap and very disfiguring Other effects are discoloration eczema and ulceration and the development of varicose veins

Treatment. Prophylaxis Active movements of the limbs in bed and early ambulation of patients diminish the incidence of thromboembolic complications As in some cases of severe debility and heart failure these measures are impracticable it may be justifiable to give prophylactic anti-coagulant therapy Tight bandages and dehydration should be avoided and antibiotics given when infection occurs

Early diagnosis helps to avoid serious complications Careful inspection of the legs for oedema or local tenderness of calf muscles should be carried out daily in elderly bed ridden cases or in any case after operation or in a debilitating illness Any unexplained rise in temperature should also put one on guard Once thrombo-phlebitis has occurred the limb is elevated and kept at rest Deep breathing is avoided and constipation and coughing checked Warmth is applied locally and if necessary analgesics are given A course of penicillin is begun and heparin 15 000 units intravenously with heparin retard 10 000 units intramuscularly are given the latter being repeated in 12 hr Phenindione (Dindevan) 100 mg is also given followed by 75 mg 12 hourly A prothrombin time is estimated in 36 hr when the effect of the last heparin injection has passed off and *this will be the guide to the dosage of phenindione* from then on Treatment need be continued only for about 10 days As soon as possible after this the leg is moved actively a firm supporting bandage or elastic stocking is used and the patient got up if his condition allows Should the condition spread or if repeated emboli are given off or suppurative thrombo phlebitis occurs ligation of the vein is necessary

CHAPTER 16

Diseases of the Respiratory System

FRANK H SCADDING

WHILE the diseases which affect the respiratory tract may be accompanied by symptoms and signs of a general nature such as malaise fever and loss of weight in the main the symptoms they produce are due to structural or functional alterations It is therefore important that the student should have a clear understanding of the essential anatomy and physiology of the system before attempting to detect departures from the normal and to interpret their significance

ANATOMY

Upper Respiratory Tract

The conducting airways above the level of the lower border of the cricoid cartilage together with the paranasal sinuses comprise the upper respiratory tract Study of the morbid conditions affecting this region has long been a speciality on its own However the dividing line between the upper and lower respiratory tracts although convenient is artificial Disease does not recognize the boundary between them Infection in the nose or throat is a frequent precursor of bronchial or pulmonary infection and the converse is also true Suppuration in the bronchi or lungs may cause infection in the nasal sinuses pulmonary tuberculosis may be complicated by tuberculous laryngitis caused by transference of infected material from the lower to the upper parts of the respiratory passages The respiratory tract should therefore be viewed as a continuous whole and where infection involves both upper and lower divisions of the tract they must be treated as far as possible at one and the same time

Air enters the larynx either through the mouth and oropharynx or through the nose and nasopharynx Examination of the respiratory system must therefore include inspection of the mouth Neglected dental hygiene is often a causal factor in lung abscess and may be an aggravating factor in such conditions as chronic bronchitis and bronchiectasis

The nose and nasopharynx lined by sensitive vascular ciliated columnar epithelium present a large surface area which warms and moistens the incoming air The surface is normally covered by a thin sheet of mucus which is constantly being wafted towards the pharynx by the action of the cilia bearing with it numerous adherent dust particles and bacteria filtered from the inspired air In the pharynx the mucus is either expectorated or swallowed

The paranasal sinuses communicate with the nasal passages Their ostia are small and relatively easily obstructed by inflammatory congestion and oedema of the mucous membrane Unless drainage can be established there exists the risk of suppuration within the sinuses or chronic infection with polyp formation

The oropharynx is lined by stratified squamous epithelium and contains abundant lymphoid tissue including the true tonsils and lingual tonsil as additional protection of the lower respiratory tract against exogenous infection

The larynx in addition to conducting air to and from the lungs is also the site of voice production At the level of the vocal cords it is narrow and may become obstructed by inflammatory or allergic oedema of the mucous membrane membranous inflammation (as in diphtheria) or by the inhalation of a foreign body Various forms of laryngeal paralysis are encountered important among them being paralysis of the left vocal cord due to involvement of the left recurrent laryngeal nerve by a mediastinal tumour or aortic aneurysm By means of the cough reflex the larynx prevents inhalation of foreign material down into the lower respiratory tract. This vagal reflex provides an important defence mechanism which can be excited by stimulation of the lower pharynx larynx the bronchial tree as far down as the larger bronchioles the parietal pleura and the external auditory meatus It is not produced by stimulation of the smaller bronchioles lung parenchyma or visceral pleura

Lower Respiratory Tract

The Trachea and Bronchi The trachea extends from the cricoid cartilage downwards and backwards to its bifurcation into the two main bronchi at the level of the lower border of the manubrium sterni It may be displaced from its midline position but is less readily compressed by virtue of the incomplete cartilaginous rings supporting it anteriorly and laterally The bronchi subsequently divide like the branches of a tree gradually tapering in calibre towards the periphery Their walls are strengthened and supported by plates of cartilage and by smooth muscles except in the small bronchi of $\frac{1}{4}$ mm or less diameter where the cartilage ceases The muscular walls of the bronchi enable them to dilate and lengthen in inspiration and to contract and shorten

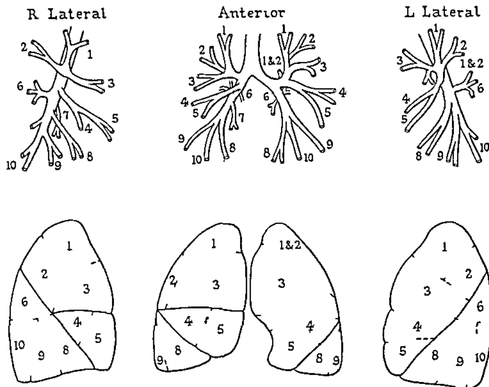


FIG 16 1 BRONCHO-PULMONARY SEGMENTS

Terminology the numbers refer both to the bronchi and the corresponding segments

Right	*Left*
Upper Lobe	Upper Lobe
1 Apical	1 Apical
2 Posterior	2 Posterior (1–2 Apico-posterior)
3 Anterior	3 Anterior
Middle Lobe	Lingula
4 Lateral	4 Superior
5 Medial	5 Inferior
Lower Lobe	Lower Lobe
6 Apical	6 Apical
7 Medial basal (cardiac)	
8 Anterior basal	8 Anterior basal
9 Lateral basal	9 Lateral basal
10 Posterior basa	10 Posterior basal

in expiration Peristaltic movements have also been described Spasm of this musculature results in the condition of bronchial asthma

The final subdivisions of the bronchi are the *terminal bronchioles* and these divide into the *respiratory bronchioles* each of which communicates with a group of *air sacs* (atria) the walls of which contain the lung alveoli

Broncho pulmonary Segments The main bronchi divide into the lobar bronchi three on the right and two on the left Each lobar bronchus then divides into *segmental bronchi* each of which supplies a broncho pulmonary segment The general anatomy of these broncho pulmonary segments is reasonably constant and time spent in learning their names and distribution will be well repaid in the clearer understanding of many of the disease processes which affect the lungs

Study of Fig 16 1 will give a clearer picture of the bronchial tree than would a lengthy verbal description It will be seen from the diagrams that the right main bronchus deviates less from the vertical than does the left main bronchus Inhaled material therefore more often enters the right side than the left The first branch from the right main bronchus is the right upper lobe bronchus It leaves the lateral wall of the main bronchus at right angles and after a short course of about 1 cm it trifurcates into the apical anterior and posterior segmental bronchi The next branch of the stem bronchus is the right middle lobe bronchus which comes off anteriorly running downwards outwards and forwards subsequently dividing into the medial and lateral segmental bronchi Almost opposite to the right middle lobe bronchus but at a slightly lower level the segmental bronchus to the apical segment of the right lower lobe leaves the stem bronchus to run horizontally backwards Thereafter the stem bronchus supplies the remainder of the right lower lobe by giving off successively the medial (cardiac) bronchus (which is not present on the left side) the anterior lateral and posterior basal segmental bronchi the last being virtually a continuation of the main stem bronchus

On the left side there is no middle lobe the latter being represented by the lingular portion of the left upper lobe The left main bronchus after passing beneath the arch of the aorta divides into two The upper lobe branch then gives off the lingular bronchus which runs downwards outwards and forwards dividing into the superior and inferior lingular segmental bronchi The upper division of the left upper lobe bronchus is then distributed to the remainder of the left upper lobe through anterior apical and posterior segmental branches as on the right side with the minor difference that the apical and posterior divisions have a short common stem—the apico posterior bronchus The left lower lobe segmental bronchi do not differ significantly from those on the right side except in the absence of a medial (cardiac) bronchus

The Pleurae The inner surface of each hemithorax including the mediastinal and diaphragmatic surfaces is lined by parietal pleura which is then reflected outwards at the hilum to invest the individual lobes of the lung as the visceral pleura It therefore forms a large invaginated serous sac the two surfaces being normally in contact but free to slide easily on each other by virtue of a film of serous fluid

The healthy lung is an elastic structure which even at the end of normal expiration is under tension or on the stretch in order to fill the hemithorax This tension or retractive force of the lung results in a subatmospheric pressure between the two pleural surfaces of some 5 or 6 cm of water in the mid respiratory position In emphysema where the elasticity of the lung is reduced the intrapleural pressure becomes less subatmospheric (less negative) and at the end of expiration may approximate atmospheric pressure The pleurae are normally impervious to air but rupture of the lung or penetrating wounds of the chest can permit air to enter the pleural space to cause a pneumothorax Similarly fluid can accumulate between the two surfaces (pleural effusion) or pus (pyothorax) or blood (haemothorax) or various combinations e g haemopneumothorax pyopneumothorax

The Thoracic Cage The bony cage forms a fairly rigid yet expansile framework containing the lungs and mediastinal structures Each hemithorax is closed above by the fascia and the soft tissues of the neck and below by the diaphragm The intercostal muscles close the spaces between the ribs and serve to elevate and evert the ribs assisted in forced inspiration or in respiratory distress by the various accessory muscles of respiration A cross section of an infant s chest is roughly circular but in the adult the transverse diameter considerably exceeds the antero posterior diameter The general configuration varies considerably—from the long thin asthenic chest with oblique ribs and an acute subcostal angle to the sthenic type in the stocky individual which is broad with obtuse subcostal angle and more horizontal ribs The greatest expansion takes place over the lower third of the thorax but in women the upper part of the chest is relatively more mobile than in men

Various congenital abnormalities may affect the thoracic cage causing local deformities e g funnel depression of the sternum anomalies of ribs absence of pectoral muscles Unless severe they

seldom cause symptoms Acquired spinal disease re sulting in scoliosis can produce asymmetry of the chest but the latter is as frequently the result of chronic unilateral pulmonary disease Some forms of congenital heart disease with considerable cardiac enlargement can also cause asymmetry Severe kyphosis also may result from chronic chest diseases particularly asthma and emphysema but may be the primary lesion resulting in gross impairment of respiratory function This occurs especially in ankylosing spondylitis where in addition the move ments of the costo vertebral joints are greatly re stricted The enlarged costo chondral junctions of active rickets (rickety rosary) are hardly ever seen to day in this country Harrison s sulcus and vary ing degrees of pigeon breast are not uncommon sometimes having resulted from a combination of rickets and repeated respiratory infections in child hood but more frequently being due to congenital deformity

RESPIRATORY FUNCTION

The primary function of the respiratory system is to obtain oxygen from the inspired air and to excrete carbon dioxide as a waste product from the blood Additional functions include voice produc tion the elimination of water vapour equivalent to 400 ml of water daily a contribution to body tem perature regulation by heat loss and the excretion of certain drugs *e g* paraldehyde ether

The enormous surface of the alveoli in direct contact with the pulmonary capillaries some 50 times the surface area of the body provides a won derfully efficient mechanism for gaseous exchange (true respiration) Molecules of oxygen and carbon dioxide are exchanged by virtue of the differences in partial pressure of the two gases in the venous blood and alveolar air The two other prerequisites for normal respiration are ventilation of the alveoli and an adequate blood flow through the pulmonary capillaries In certain diseases the alveolar mem brane itself becomes thickened by fibrous tissue *e g* in the various forms of diffuse pulmonary fibrosis or by pulmonary oedema as in cardiac failure and the diffusion of gases is impaired Because carbon dioxide diffuses much more readily than oxygen the clinical problem produced by such conditions is that of anoxaemia rather than carbon dioxide retention

More commonly however diseases of the lungs interfere with the free transfer of air to and from the alveoli resulting in diminished alveolar ventila tion (hypoventilation) If sufficient in degree this may cause both anoxaemia and carbon dioxide re tention Efficient ventilation demands flexibility of the thoracic cage conducting airways free from obstruction elasticity of lung tissue effective respiratory muscles and a regular rhythmic action of the respiratory centre These factors singly or together may be impaired by many disease pro cesses and consequently hypoventilation may be a feature of several clinical conditions

Normal inspiration is effected by active contrac tion of the respiratory muscles which increase the volume of the thorax Air flows freely in the lungs being elastic distend and the smooth muscle in the bronchial walls relaxes to increase their lumen Normal expiration on the other hand is a purely passive act achieved by the elastic recoil of the lungs and chest following inhibition of the in spiratory muscles It is a relatively weak force and any obstruction to the free exit of air from the lungs tends to cause prolongation of the time required to return the chest to its original end expiratory position Generalized narrowing of the bronchial tree by spasm as in asthma or by mucosal swelling as in chronic bronchitis prolongs expiration and if of sufficient degree will result in deficient alveolar ventilation because of the time factor The body s first response to such conditions is to increase the force of expiration by deepening inspiration and so to increase the retractive force of the lungs until it is sufficient to equalize the inspiratory and ex piratory tidal volumes once more A state of pul monary over inflation develops which in time may be followed by degeneration and rupture of the alveolar walls the condition known as emphysema It will be realized that the important factor in ventilation is not so much the volume of air that can be inspired (vital capacity) but the volume of air that can be got in and out again in the required time Similarly reduction of the lung volume may cause little disability because the significant factor is not the total volume of the lungs but the propor tion of the total which is freely ventilated

Effects of Posture The supine position reduces the capacity of the lungs particularly the functional reserve volume due to elevation of the diaphragm The assistance of gravity in displacing the abdomi nal viscera downwards in inspiration is also lost and a patient whose breathing is already seriously embarrassed cannot lie flat in bed because of this further restriction in his respiratory reserve but has to be propped up into the sitting position (orthop noea) This position is of additional importance where there is excessive secretion in the lungs or bronchi The diminished basal excursion and the

less effective cough engendered by restricted diaphragm movement may permit its retention with consequent atelectasis and infection

For the assessment of respiratory function a wide variety of tests is now available but many of them are complicated and beyond the scope of this book. However measurement of the volume of the subdivisions of the lung is relatively easily performed with a spirometer and diagrammatic representation of a normal spirogram is shown in Fig 16 2

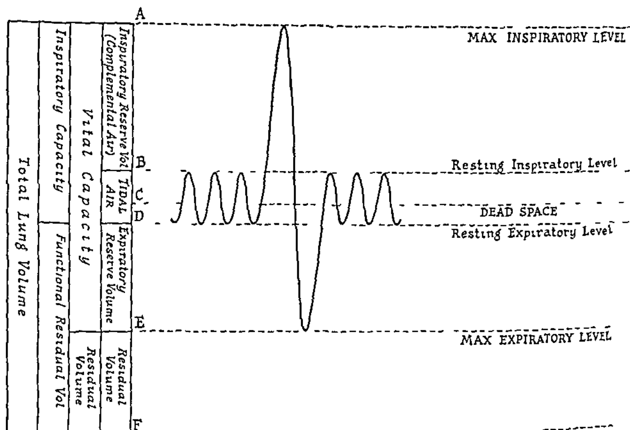


FIG 16 2 NORMAL SPIROGRAM

Tidal Air (B–D) = Volume of air breathed in and out during normal quiet respiration (N=350–500 ml)

Inspiratory Reserve Volume or Complemental Air (A–B) = Volume of air which can be inspired by voluntary effort at end of normal inspiration (N=1 500–3 000 ml)

Expiratory Reserve Volume or Reserve Air (D–E) = Volume of air which can be expired by voluntary effort after normal expiration (N=1 200–1 500 ml)

Residual Volume (E–F) = Volume of air remaining in the lungs at the end of a maximum expiratory effort (N=1 200–1 500 ml)

Functional Residual Volume (D–F) = Volume of air in the lungs at the end of a normal expiration (N=2,500–3 000 ml)

Vital Capacity (A–E) = Volume of air which can be expired by voluntary effort after a maximal inspiration (N=3 000–5 000 ml)

Dead space Air (C–D) = That part of the tidal air occupying the conducting air passages and taking no part in gaseous exchange (N=25–30 per cent of the tidal air=150–170 ml)

Total Lung Volume (A–F) = Volume of air contained in the lungs at the end of a maximal inspiration (N=5 500–6 000 ml)

SYMPTOMS OF RESPIRATORY DISEASE

Infections of the respiratory system as infections elsewhere are frequently accompanied by general symptoms of toxaemia such as malaise headache limb pains fever anorexia and loss of weight but there are five cardinal symptoms particularly associated with chest disease These are *cough expectoration blood spitting (haemoptysis) dyspnoea* and *pain*

Cough A frequent dry unproductive cough is an early symptom of irritation of the mucosa of the respiratory tract and is common in the early stages of pharyngitis laryngo tracheitis and bronchitis whether of infective origin or due to physical agents such as excessive smoking Characteristically cough is paroxysmal in whooping cough when it occurs particularly at night in the first week of the illness and is often followed by vomiting Paroxysms of coughing may also occur with asthma bronchial neoplasms or when a foreign body is present in a bronchus A productive cough is one which results in the removal of sputum from the air passages and this may be swallowed or expectorated Change of posture may precipitate cough in bronchiectasis or lung abscess Occasionally the sound of the cough is of diagnostic significance as in the brassy cough associated with compression of the trachea or a main bronchus

Sputum Important and sometimes diagnostic information may be obtained from examination of the sputum and both its quality and quantity should be noted It varies enormously from scanty odourless viscid mucus in the early stages of bronchitis or pneumonia to several ounces daily of foul smelling pus in pulmonary suppuration A greenish colour usually indicates stagnation Muco purulent sputum occurs in many lung diseases notably pulmonary tuberculosis with breaking down of the lung tissue and in the resolution stage of bronchitis and pneumonia Other macroscopic features that may be noted are the presence of blood carbon particles in town dwellers and particularly in coal miners and very occasionally such things as bronchial casts hair pieces of chalk or necrotic lung tissue Microscopy and culture will yield further information concerning the cells bacteria parasites and dust particles

Haemoptysis The differentiation of haemoptysis and haematemesis in practice is usually straightforward if the patient is questioned closely Where doubt exists it should be borne in mind that haematemesis is usually preceded by a feeling of nausea or faintness and the rejected material is acid in reaction and coffee grounds in appearance unless the blood is coming from the oesophagus or is very large in amount The patient with haemoptysis frequently experiences a salty taste in the mouth and then coughs up a variable quantity of bright blood which is alkaline in reaction A previous history of dyspepsia or chest symptoms is also helpful in differentiation but occasionally the answer is revealed only by subsequent investigations Blood spitting in which the blood is coming from the upper respiratory tract is called pseudo haemoptysis True haemoptysis may occur in almost every disease affecting the respiratory tract and no purpose would be served by appending a long list of such conditions In general acute inflammatory diseases give rise only to flecking or staining of the sputum and the blood may be altered in the early stages of a pneumonic process to give the characteristic rusty sputum Frank haemorrhage is a common feature of the more chronic pulmonary diseases such as pulmonary tuberculosis bronchiectasis lung abscess and new growths and may occasionally be fatal It is also not uncommon in certain cardiac disorders with or without pulmonary infarction notably in mitral stenosis

Dyspnoea It is important to remember that breathlessness a common symptom of pulmonary disease may also be a prominent feature in cardiac metabolic haematological and nervous disorders Dyspnoea in chest disease is seldom due to an overall reduction in functioning lung tissue A patient with only one lung may have no difficulty in breathing whereas another with a comparatively small inflammatory lesion occupying perhaps one segment may do so More important in its production is the direct stimulation of the respiratory centre by an excess of carbon dioxide in the blood resulting especially from hypoventilation and reflex stimulation of breathing via the vagus in the many conditions in which pulmonary congestion or increased rigidity of pulmonary tissue are features Reflex dyspnoea such as occurs in pneumonia pulmonary atelectasis neoplastic infiltration etc is characterized by rapid and shallow respiration whereas in the chemical dyspnoea due to failure of elimination of carbon dioxide or to metabolic acidosis the main feature is the increased depth of breathing with or without some increase in rate (hyperpnoea)

Anoxaemia as a cause of dyspnoea in pulmonary disease has been exaggerated in the past Stimulation of breathing by reflexes originating in the sino aortic chemoreceptors in response to anoxaemia does occur but is of trivial importance compared with the effect of a raised carbon dioxide tension in the blood In advanced chronic pulmonary disease particularly emphysema however these reflexes may

assume *greater importance* The impaired pul monary ventilation causes progressive accumulation of carbon dioxide in the blood and the respiratory centre may eventually become insensitive to it Con trol of respiration is then largely dependent upon these anoxic reflexes Under these circumstances if oxygen is given in high concentration the anoxia is *relieved* and breathing may then cease altogether the carbon dioxide will then rise still further and *may reach toxic levels Oxygen therapy therefore* in such patients although necessary requires care ful supervision and it is usually wiser to employ it intermittently or with comparatively low rates of flow (2–3 litres/min) until such time as the pul monary ventilation can be sufficiently improved to remove the excess of carbon dioxide If this can be *achieved* the carbon *dioxide tension falls* and the *respiratory centre regains its sensitivity to it* Oxy gen therapy can then be continued in sufficient concentration to produce full saturation of the arterial blood

Further information as to the type of dyspnoea may be gleaned from the patient s history and its severity *may be judged from the degree* of effort required to produce it He may describe attacks of expiratory difficulty suggesting asthma or a per sistent wheezy dyspnoea as in chronic bronchitis or paroxysms of intense dyspnoea at night precipitated by the recumbent position such as occur with pul monary congestion and oedema due to left ven tricular failure or mitral stenosis (paroxysmal noc turnal dyspnoea)

Pain The lungs and visceral pleura are devoid of pain sense and extensive disease of the lungs may exist without causing pain The parietal pleura how ever is extremely sensitive and if irritated or in flamed (*i e* pleurisy) gives rise to characteristic pleural pain This is a sharp *stabbing pain related* to respiratory movement and agonizing on cough ing It is usually referred to the chest wall over the area *of inflammation* and is worse in the lower lateral region of the chest where movement is greatest In diaphragmatic pleurisy the pain may not only be felt in the lower chest wall but also may be referred via the phrenic nerve (C3 4 and 5) to the neck and shoulder on the same side or via the lower intercostal nerves to the upper abdomen. *The severity of pleural pain* is such as to cause the patient to breathe as shallowly as possible to sup press his *cough if he can* and *to clutch his chest* tightly to minimize its movement if he must cough The pain is probably due to increased tension in and stretching of the parietal pleura during the acute stage of inflammation and not to the rubbing together of the two inflamed pleural surfaces since *a pleural rub can be heard long after the pain has subsided*

Pain of a different type is experienced by a patient in the early stages of acute tracheo bronchitis It is described as a soreness or raw feeling behind the upper part of the sternum unrelated to respiratory excursion but aggravated by the *frequent dry cough* which accompanies this condition

A constant severe ache in the upper part of the chest and lower neck radiating down the arm is sometimes the first symptom of an apical broncho genic carcinoma involving the brachial plexus and periapical bony structures (Pancoast s tumour) Pain may also arise in the chest wall *in cases* of fractured rib or herpes zoster Very often however chest pain is *not* associated with any pulmonary abnormality but with disease affecting the cardio vascular gastro intestinal skeletal or central ner vous system Its character and significance are dis cussed in more detail in the respective sections of this book

EXAMINATION OF THE RESPIRATORY SYSTEM

History An accurate account of the patient s complaints in chronological order without prompt ing is the first step and its importance cannot be *over stressed This is then amplified* by the answers to leading questions concerning general symptoms and the five cardinal symptoms already mentioned information being sought as to their presence dura tion type and severity

Previous History Enquiry *should be made as to* previous respiratory disorders including the child *hood* illnesses of measles and whooping cough which may mark the onset of bronchiectasis A ten dency to frequent sore throats nasal catarrh recur rent bronchitis or asthma may be *revealed* and a note should be made of such conditions as pneu monia pleurisy tuberculosis chest injuries or operations *on the upper respiratory tract*

Evidence of previous contact is important in the *infectious diseases* and in tuberculosis in particular

The occupational history may provide a clue to diagnosis in certain dust diseases of the lung (pneu moconioses) and may also point to *remediable* aggravating if not causal factors in such conditions as *chronic bronchitis and asthma*

Family History The contact history will have yielded some information on the health of the other members of the family but further efforts *should be* directed to discovering any family tendency to *tuberculosis recurrent bronchitis* and allergic con ditions *e g* hay fever

Clinical Examination

It is impossible to assess the abnormal signs in the chest of a patient who is shivering with cold The examiner s hands should be warm and the examination should be carried out in a warm room preferably in daylight All clothes should be removed above the waist and the semi recumbent position will be found both convenient for the examination and comfortable for the patient

General Examination

This includes a general appraisal of the patient s build colour and mental attitude The body temperature should be noted along with the rate rhythm and depth of respiration and the rate rhythm and quality of the pulse at both wrists Special attention should be given to the detection of cyanosis and clubbing of the fingers

Cyanosis The presence of blood containing an excess of reduced haemoglobin in the capillaries of the skin and mucous membranes imparts to these surfaces a bluish colour Peripheral cyanosis is commonly seen in patients susceptible to cold and in other cases where a sluggish circulation exists locally Central cyanosis in which there is incomplete oxygenation of the blood in the lungs is difficult to detect in its lesser degrees and requires careful scrutiny of the nail beds and mucous membrane of the mouth after ensuring that the patient is thoroughly warm Pulmonary causes of cyanosis include all the causes of hypoventilation and impaired diffusion of oxygen across the alveolar membrane It may also result from a veno arterial shunt in certain cases of congenital heart disease *e g* Fallot s tetralogy In so far as cyanosis becomes detectable only when 5 g/100 ml of reduced haemoglobin are present in the blood it will be obvious that a severely anaemic patient cannot become cyanosed even though he may be anoxic Occasionally the presence in the blood of abnormal pigments (methaemoglobin and sulphaemoglobin) may cause a central type of cyanosis (chemical cyanosis ') and this should be considered when no obvious cardiac or pulmonary lesion is detected

Clubbing of the Fingers (Plate 16 1) This is often a useful indication of chronic pulmonary disease although the mechanism of its production remains obscure The first sign of clubbing is filling in of the angle which normally exists between the proximal part of the nail and the skin The tissues of the nail bed become loosened by congestion and oedema so that the proximal edge of the nail can readily be felt when it is rocked longitudinally The skin overlying the nail bed assumes a pink shiny atrophic appearance Following these changes the nail itself becomes increasingly curved both in the transverse and longitudinal planes (parrot bill clubbing) and in the severest form there is general expansion of the whole of the end of the finger (drum stick clubbing) Similar changes usually less in degree occur in the toes and occasionally the distal ends of the long bones may enlarge as a result of the laying down of new bone and the joints themselves become swollen (pulmonary osteo arthropathy) The commonest pulmonary diseases giving rise to finger clubbing are those associated with chronic suppuration *i e* lung abscess bronchiectasis and empyema Lesser degrees are common in long standing bronchitis and emphysema and carcinoma of the bronchus but it is only seldom a feature of uncomplicated pulmonary tuberculosis

It must be remembered that clubbing is not specific to pulmonary disease Severe forms of it are encountered in patients with congenital heart disease and lesser grades in such apparently unrelated conditions as subacute bacterial endocarditis cirrhosis of the liver and steatorrhoea There is also a familial form and unilateral clubbing is occasionally seen with vascular abnormalities affecting one limb

Examination of the Upper Respiratory Tract

The airway through each nostril is tested by temporary occlusion of first one side and then the other Tilting the tip of the nose with the finger allows a limited inspection of the anterior nares and if symptoms point to the nose further examination by means of a nasal speculum will be required Deflection of the septum to one side is very common The presence and character of any nasal secretion the state of the mucous membrane source of bleeding polypi or structural abnormalities should be noted Any swelling or pain on pressure or percussion over the sinuses will require further investigation

General examination of the mouth teeth and gums is followed by inspection of the palate fauces and pharynx The size and condition of the tonsils requires special attention and muco pus in the nasopharynx indicates the need for fuller examination of the nasopharynx and posterior nares

The larynx and vocal cords can be seen only by means of reflected light from a laryngeal mirror or through a largyngoscope The main symptoms for which such examination is required are a persistent irritating dry cough stridor and hoarseness Stridor is heard when there is partial obstruction of the larynx trachea or a main bronchus and hoarseness may be caused by benign or malignant neoplasms specific or non specific laryngitis or by paralysis of the vocal cords The left recurrent

laryngeal nerve is often involved in the mediastinum by pressure from an enlarging tumour particularly a bronchial carcinoma and the first symptom may be hoarseness due to paralysis of the left vocal cord

Before proceeding to examination of the chest the neck should be examined The central position of the trachea should be verified thyroid abnormalities noted and a careful search made for enlarged lymph nodes particularly in the supra clavicular fossae

Examination of the Chest

Certain general surface markings should be borne in mind during the examination in order to interpret the physical signs correctly and to assist in the localization of disease in the lungs Because of the obliquity of the first rib the apex of each lung extends some 1–1½ in up into the root of the neck From the neck of the first rib the line marking the medial border of each lung runs downwards and inwards to meet its opposite number in the midline at the lower border of the manubrium sterni *On the right side* the line continues vertically downwards to the level of the 6th costal cartilage and then in the mid respiratory position turns outwards and downwards to cross the 8th rib in the mid axillary line the 10th rib in the scapular line and the 11th rib at the vertebral column *On the left side* the line proceeds vertically down as far as the 4th costal cartilage and then deviates to the left and downwards to the level of the 6th costal cartilage a short distance outside the left border of the sternum There after its course is the same as on the right but at a slightly lower level The lower limit of the pleura is some 3 in below that of the lung in the mid axillary line and some 1½ 2 in in the mid clavicular and scapular lines The oblique fissure on either side can be represented by a line from the 3rd dorsal spine running along the 5th rib or intercostal space to the 6th costo chondral junction 2–4 in from the midline This corresponds roughly to the vertebral border of the scapula when the arm is abducted to a right angle *The transverse fissure* is marked by a horizontal surface line from the 4th costal cartilage outwards to meet the oblique fissure in the mid axillary line Picturing these lines the student will realize that the right middle lobe occupies an anterior and lateral position and cannot be examined from behind that only a small portion of the upper lobe can be examined from the back and that portions of all three lobes are accessible in the axillary line The vertebral spines can be identified by counting downwards from the vertebra prominens (C7) and the rib and intercostal spaces by starting at the angle of Louis (2nd costal cartilage)

The traditional method of chest examination trains the student to use his eyes first then his hands and finally his ears The sense of smell also occasionally yields useful information The orderly sequence of inspection palpation percussion and auscultation cannot be bettered and should be practised as a normal routine

Inspection Attention should first be paid to the general configuration and symmetry of the chest, local or general deformities skin lesions prominence of superficial veins and the rate and character of respiration The apex beat normally in the 5th left intercostal space 3½–3¾ in from the midline is often visible in healthy slim individuals Its position should be checked by measurement and any other cardiac pulsation noted The degree of movement and expansion of the thorax should then be observed from the foot of the bed in quiet respiration and during deep inspiration The expansion from the full expiratory to the full inspiratory position can be recorded with a tape measure Generalized pulmonary disease tends to diminish the movement of the chest on both sides but if one side moves less than the other that will be the abnormal side provided skeletal deformity can be excluded

Palpation Palpation confirms and elaborates what has been learned by inspection Any deviation of the trachea or apex beat is verified and a detailed examination is made of any local abnormality Tumours should be tested for consistency tenderness fluctuation pulsatility and adherence to underlying structures The direction of blood flow in abnormal veins should also be determined The excursion of the upper part of the chest is observed by laying the flat hands lightly over the pectoral and subclavicular regions one hand on each side at the same time Even slight degrees of impaired movement can be detected in this way Movement and expansion of the lower part of the chest is examined by lightly embracing the lower ribs fingers lying in the intercostal spaces and the extended thumbs just touching in the midline Contraction of the intercostal muscles with elevation and eversion of the ribs is readily appreciated and the degree of lateral expansion is indicated by separation of the two thumbs Not infrequently in patients with emphysema and in elderly subjects the chest seems to be lifted forwards and upwards as a whole with little or no lateral expansion Diminished movement on one side can result from spinal deformity muscular paralysis or a wide variety of pulmonary conditions including pneumonia tuberculosis atelectasis pleural effusion and pneumothorax In fact any pathological process which diminishes the amount of air entering one lung will impair the movement of that side of the chest

Vocal fremitus or *tactile fremitus* is the vibra



Clubbing of the Fingers

Radiograph of the Normal Chest

Plate 16 1

Generalized Cystic Bronchiectasis

Fusiform and Saccular Bronchiectasis of the Left Lower Lobe

Plate 16 2

tion felt by placing the hand on the chest wall while the patient says '99' or other resonant syllables Similar regions on the two sides are compared by using the palm of the hand and individual inter costal spaces by the ulnar side of the palm

In the normal chest the vibration is usually more intense over the right upper lobe than the left and equal in intensity over other symmetrical areas It is dependent upon the resonance of the spoken voice and may be hardly appreciable in women with high pitched or soft voices Similarly it is diminished generally by a thick chest wall

In disease vocal fremitus is diminished at all areas by hoarseness or aphonia pulmonary emphysema and diffuse pulmonary fibrosis It is decreased on one side or locally by pleural thickening and atelectasis associated with persistent bronchial obstruction and it is greatly diminished or absent dependent on their size over a pneumothorax or pleural effusion For practical purposes it is in creased in only one condition *i e* consolidation of the lung without bronchial obstruction (pneumonia)

Rhonchial fremitus is the vibration transmitted to the hand by low pitched rhonchi arising in the larger bronchial tubes during bronchitis It is independent of the spoken voice and inconstant not accom panied by pain and usually vanishes temporarily after coughing

Pleural fremitus is a rubbing or scraping sensation felt by the hand during respiratory excursion in cases of dry pleurisy corresponding to the pleural rub In the acute stage of pleurisy it is accompanied by pain which is aggravated by firm pressure of the hand and is usually felt over the lower part of the chest where movement is greatest

Percussion. Direct tapping of the chest wall yields little useful information In malnutrition or any disease causing severe wasting a sharp tap over the pectoral muscles may cause fibrillary contractions (myotatic irritability or myoidema) but it is of little diagnostic importance as it can be elicited in normal thin individuals

Indirect percussion is performed by placing one finger of the left hand on the chest and striking it sharply with the tip of the right middle finger the right wrist being alternately flexed and extended in rapid succession The technique requires practice and heavy blows must be avoided as they fail to detect the lesser abnormalities

The Normal Chest The percussion note emitted from normal lung is resonant. Word descriptions of sounds are seldom helpful to the student and he is urged to familiarize himself with normal resonance by frequent examination of healthy chests The average normal note can be heard on percussion in the right axilla Direct percussion of the clavicle or indirect percussion in the subclavicular areas also gives a resonant note but less resonant than in the axilla Percussion over the lung bases behind gives a more resonant note than is obtained at either of the two previous sites This is to be expected because of the conical shape of the lung Posteriorly the lower limit of each lung can be reasonably accurately determined by the change from resonance to non resonance while percussing from above downwards and by noting the limit of resonance in full expiration and inspiration diaphragmatic excursion can be assessed Anteriorly percussing each intercostal space in turn from above down wards the extent of liver and cardiac dullnesses will be noted There is no sharp demarcation however and only a considerable increase or decrease in these non resonant areas is of significance In the left lower axilla the transition is from normal lung resonance to tympany over the gas bubble in the stomach The tympanitic note is high pitched hollow and drum like similar to the note of a kettle-drum and is indicative of air or gas under pressure

In Disease The percussion note may be more resonant than normal (hyper resonant) or less resonant than normal (impaired note dullness) the most extreme degree of impaired resonance being stony dullness since it resembles the sound produced by percussing a brick wall

Having made himself conversant with normal resonance and tympany the student should next learn to recognize hyper resonance and stony dull ness In general it will be found that a more resonant note is lower in pitch and louder whereas with increasing dullness the note becomes higher in pitch and less loud. If he does not possess a musical ear the student need not feel depressed at failing to appreciate changes in pitch since with practice he will detect a "sense of resistance which is least over hyper resonance and greatest when the note is stony dull Morbid conditions which increase the volume of air in the chest give a hyper resonant note thus generalized hyper resonance with diminution or absence of the normal cardiac and liver dullnesses occurs in emphysema Hyper resonance on one side only is occasionally due to unilateral emphysema or a large air-containing cyst but more commonly to a pneumothorax and should the air in the pleural space be under positive pressure the note may become tympanitic Conditions which diminish the volume of air in the chest are usually associated with varying degrees of decreasing resonance Extreme dullness is characteristic of fluid in the pleural space while lesser degrees of impaired resonance are given by consolidation of the lung atelectasis pulmonary oedema infiltration or

fibrosis and by pleural thickening When the pleural space contains both air and fluid (hydropneumo thorax) the two extremes of resonance are encoun tered on the same side of the chest the note being stony dull over the fluid and hyper resonant over the air *The dividing line between them is hori zontal* and its level can be altered by changing the patient s position

Auscultation *Breath Sounds* It is probable that the breath sounds heard with the stethoscope applied to the chest actually arise at the vocal cords and that their characteristics depend on the type and condition of the tissues through which the sounds are transmitted to the ear Even in healthy subjects there is a considerable range of normality which can be learnt only by experience and the beginner *should ignore minor changes unless they are accom* panied by other abnormal physical signs The features to note about the breath sounds are the loudness or intensity the duration—particularly of expiration—and the pitch

The Normal Chest Auscultation over normally functioning lung alveoli at some distance from the source of sound *e g* in the right axilla will demon strate normal *vesicular* breathing It is a gentle moderately low pitched rustling sound The whole of inspiration but generally only the first part of expiration can be heard with no appreciable pause between them If the stethoscope is next applied to the trachea loud *bronchial breathing* will be heard In this situation the breath sounds are very loud *because the chest piece is very near to the source* of sound but it will also be noted that (*a*) the whole of expiration is easily heard following inspiration after a short pause (*b*) the pitch is higher and (*c*) there is a *hollow* quality to the sounds Loudness is not a specific feature of bronchial breathing nor is softness a necessary feature of vesicular breathing Breath sounds may be very weak yet bronchial by virtue of their high pitch prolonged expiration and hollow quality and vesicular breath sounds are nor mally loud and harsh in children With the stetho scope in one or other sub clavicular region as might be expected the breath sounds are intermediate between bronchial and vesicular (broncho vesicular or vesicular bronchial) Thus the whole of expira tion is usually audible and the pitch of one or other phase of respiration is raised to that of bronchial breathing Further exploration of the normal chest will reveal bronchial breathing over the upper part of the sternum and over the upper four dorsal vertebrae behind because of the proximity of the trachea and bronchial or broncho vesicular breathing in the interscapular regions *because of the proximity of the* main bronchi

In Disease The intensity of the breath sounds irrespective of their quality may be diminished by *any morbid process which interferes with free ven* tilation of the alveoli *e g* in bronchial obstruction paralysis of respiratory muscles emphysema oedema of lung or fibrosis of lung Similarly the *sounds may be damped down by obesity* thickened pleura or fluid or air in the pleural space If suffi cient in degree such conditions may render the breath sounds completely inaudible Bronchial breathing heard at an abnormal site depends upon increased conduction of the tracheal breath sounds When lung tissue is rendered more solid by inflam matory exudate (*consolidation*) neoplastic invasion or atelectasis bronchial breathing may be heard provided the bronchi in that area are patent It is important to realize however that *the volume of lung involved must be considerable and near the* surface A layer of healthy lung tissue 1 in or more thick between the diseased area and the surface may prevent any abnormality being detected *Tubular breathing* is the easiest form of bronchial breathing to recognize and is heard particularly well over con solidated lung as in pneumonia or over massive collapse of the lung It is of very high pitch and whiffing in character *Cavernous* breathing is an other variety of bronchial breathing but low in pitch very hollow and somewhat spooky in nature In its most intense form it has a deep echo ing quality similar to the sound produced by blow ing over the mouth of an empty bottle and is called *amphoric breathing* Cavernous or amphoric breath ing *is occasionally heard over* a large superficial pulmonary cavity with a patent communicating bronchus particularly when the cavity is surrounded by consolidated lung

Vocal Resonance *The Normal Chest* The spoken voice is heard loudly and distinctly over the larynx and trachea but over normal lung th sound is muffled and the words are indistinct Vocal resonance is tested by listening while the patient says 99 as in testing vocal fremitus and l ke the latter is usually greatest over the right upper zone

In Disease Over consolidated lung in particular vocal resonance may be increased so that the sound is louder and the syllables are heard distin tly (bronchophony) In its highest degree whispered words are clearly audible (whispering pectoriloquy) In so far as these two signs depend upon the same structural changes as produce bronchial breathing they may be expected and are usually found when ever the latter is detected Whispering pectoriloquy is a more sensitive and useful test since it is often present when the breath sounds although bronchial are distant or greatly diminished

Voice conduction is diminished by the *same*

Ancillary Methods of Examination

The nasopharynx and larynx are examined in reflected light by using a head mirror and a laryngeal mirror (indirect laryngoscopy) Under anaesthesia a laryngoscope may be used for direct inspection of the larynx Diminished translucency of the para nasal sinuses suggesting inflammation fluid or other abnormalities can be detected by trans illumination in the dark or by radiography

Bronchoscopy Under local or general anaesthesia the lumen and walls of the trachea and major bronchi are examined through a bronchoscope It is essentially a hollow metal tube of appropriate diameter fitted with suitable lighting

Radiography of the Chest. Radiological examination of the lungs is essential in the investigation of pulmonary disease It will detect diseases like pulmonary tuberculosis much earlier than physical examination and not infrequently it reveals quite extensive pathological lesions which because of their position or nature give rise to no abnormal signs The postero anterior radiograph is the usual view taken but for accurate localization of a lesion lateral and sometimes oblique films are also necessary Considerable experience is required for their interpretation as they are but shadows and a diagnosis may be reached only by consideration of the clinical state the situation and type of shadow and the results of laboratory tests

Inspection of a chest radiograph should be *methodical in order to avoid error* A *normal film* is shown in Plate 16 1 and the following routine is suggested —

The Thoracic Cage Spinal or rib deformities injuries or abnormalities may be revealed

The Diaphragm The position and contour of the two halves of the diaphragm are noted The right is normally ½ in higher than the left both being smoothly convex upwards The costophrenic angles are sharp and clear Obliteration of these angles or peaking of the diaphragm results from pleurisy or pleural effusion Both halves are displaced upwards by a raised abdominal pressure and downwards in emphysema Upward displacement of one half is produced by pulmonary atelectasis or fibrosis on that side or by paralysis of the phrenic nerve The excursion of the diaphragm can be assessed by comparing two radiographs one taken in inspiration and the other in expiration or by observing the movements on a fluoroscopic screen A paralysed hemi diaphragm is high in position and ascends during inspiration particularly if this is rapid and vigorous as during sniffing (paradoxical movement)

The Mediastinal Shadow Any displacement is at once evident by noting the position of the trachea and heart shadow The shape of the heart and provided there has been a distance of 6 ft between the X ray tube and the film its size can also be assessed Widening of the mediastinum may be caused by benign or malignant tumours cysts lymph node *enlargement etc*

The Lung Fields The hilum of each lung casts an irregular somewhat triangular shadow from which the broncho vascular striations radiate fan wise These striate shadows are vascular and cross each other decreasing in width and intensity towards the periphery They are heaviest in the inner part of the lower zones The interlobar fissures are sometimes visible particularly in lateral films For the purpose of description the lung fields are divided into radiological zones the upper zone above the 2nd costal cartilage the middle zone between the 2nd and 4th costal cartilages and the lower zone below the 4th costal cartilage The translucency of the lung fields varies with the amount of contained air relative to lung tissue Increased translucency is seen in emphysema air-containing cysts and pneumothorax but the majority of pulmonary diseases being associated with an inflammatory exudate into the alveoli or cellular infiltration cause diminished aeration and consequently decreased translucency

Bronchography Normal bronchi are not demonstrable on plain radiographs Films are taken after a radio opaque substance usually an iodized oil *e g* Dionosil has been injected into the bronchial tree via the nose mouth or cricothyroid membrane It is most helpful in the diagnosis of bronchiectasis (Plate 16 2) but is useful also in demonstrating bronchial obstruction beyond the range of bronchoscopic vision and abnormalities in distribution and position of the bronchi themselves

Tomography A special radiological technique whereby serial sections or planes of lung may be seen with minimal interference from structures in other planes It is particularly useful in the demonstration of cavities within an apparently solid lesion

Examination of the Blood

Blood Count Helpful diagnostic information can often be obtained from the blood count particularly the number and type of white blood cells Pyogenic infections as elsewhere in the body tend to cause a polymorphonuclear leucocytosis Tuberculosis seldom alters the blood count to a significant degree virus infections tend to cause a leucopenia An eosinophilia suggests an allergic or parasitic disease

Erythrocyte Sedimentation Rate (E.S R or

fibrosis and by pleural thickening When the pleural space contains both air and fluid (hydropneumothorax) the two extremes of resonance are encountered on the same side of the chest the note being stony dull over the fluid and hyper resonant over the air The dividing line between them is horizontal and its level can be altered by changing the patient s position

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in 2 or 3 days but more commonly secondary infection supervenes nasal discharge becomes mucopurulent and may continue for several days even though the constitutional symptoms may have subsided

Complications. Local spread of infection via the Eustachian tubes may produce a simple catarrhal deafness or in the stage of secondary infection an acute purulent otitis media Similarly pyogenic infection of the paranasal sinuses usually maxillary or frontal may complicate the picture with local pain tenderness and sometimes swelling over the affected sinus The infection may descend to a variable extent to cause laryngitis tracheitis bronchitis or pneumonia

Differential Diagnosis This is seldom difficult but must include influenza the various forms of allergic rhinitis exacerbations of chronic sinusitis and in children the early stages of the acute specific fevers especially measles

Treatment 1 *Preventive* Avoidance of contact is the only reliable measure and this is impracticable The early stage is very infectious and the patient should if possible stay at home in self imposed isolation This advice is usually ignored If close contact with young children or elderly subjects is inevitable a mask containing cellophane should be worn The nose and mouth should always be covered during coughing and sneezing and paper handkerchiefs which can be burned immediately after use are advisable Evidence that autogenous or stock anti catarrhal vaccines reduce the incidence of colds is lacking

2 *Curative* No specific treatment is yet available Rest in a warm but well ventilated room for 2 or 3 days is advisable Bed rest will be dictated by the severity of the constitutional symptoms Diet is unimportant but hot drinks should be taken freely Aspirin 0 6 g (10 gr) t d s or compound tablets of aspirin phenacetin and caffeine (tabs A P C) can be given for the headache and the nasal congestion can be helped by menthol inhalations or a nasal spray of 1 per cent ephedrine in saline Convenient proprietary nasal decongestants are available in the form of vapour (Benzedrex inhaler) or spray (Neophryn nasal spray) These measures are purely symptomatic but afford temporary relief pending the natural resolution of the disease

Epistaxis

Bleeding from the nose is a common event and in most cases the haemorrhage is from the antero inferior part of the septum known as Little s area Trauma is the commonest precipitating factor including the habit of nose picking and violent nose blowing particularly while the mucous membrane is congested as during a cold Other local causes include a foreign body benign and malignant neoplasms and fractured skull Hypertension venous or arterial may give rise to severe epistaxis and it may also be a feature of the various haemorrhagic diseases

Treatment Slight cases need no treatment unless bleeding is recurrent More severe haemorrhage can be arrested by compressing the nose between finger and thumb for 10–15 minutes with the patient semi recumbent Local application of adrenaline or snake venom on cotton wool to Little s area or cauterization is also effective If bleeding continues or if the site is not obvious the nose should be cocainized and packed from behind forwards with ribbon gauze soaked in 1 1 000 adrenaline Alternatively a finger cot may be inflated in the nose through an attached catheter Severe and recurrent cases should receive full clinical examination and haematological investigation to exclude the general disorders already noted If none is found the advice of an ear nose and throat surgeon should be sought

Nasal Allergy

Some individuals are born with or acquire an extreme sensitivity to certain foreign substances usually of a protein nature (allergens) In such a sensitive individual exposure to even a minute dose of the allergen may evoke a violent reaction It is thought that the allergen stimulates the production of antibodies in the allergic individual and that the allergen antibody reaction causes local and general symptoms by the liberation of histamine The allergen may gain access to the body by direct contact by ingestion by inhalation or by inoculation and for various reasons not yet known the brunt of the ensuing reaction falls upon various tissues in different individuals A wide variety of clinical features may therefore be produced among the commonest being skin eruptions hay fever vasomotor rhinitis and asthma More than one syndrome may occur in the same subject *e g* hay fever and asthma or a combination of eczema and asthma and a hereditary influence is not infrequently suggested by the family history In some instances the offending substance can be readily identified *e g* pollen in hay fever other patients learn to avoid various articles of food *e g* eggs strawberries shell fish etc because of skin eruptions or gastro intestinal upsets which follow their consumption A host of allergens one or more of which may provoke reactions in hypersensitive patients could be compiled prominent among them being animal dander feathers house dust and cosmetics but not infrequently an allergic basis for the disease rests upon supposition only either because no single allergen can be identi

B S R) This is a non specific test of some value in assessing the activity of pulmonary tuberculosis and as an indication of progress A normal reading however does not exclude active disease

Complement fixation tests agglutination tests and other haematological investigations are occasionally required and will be discussed in their appropriate sections

Examination of the Sputum

The general features of sputum including the colour odour consistency and volume have already been noted For its bacteriology a smear from a morning specimen is stained and examined and cultures set up on selective media both aerobically and anaerobically If no sputum is available cultures can be made from laryngeal swabs or the fasting gastric juice The presence of *M tuberculosis* is always abnormal There are however several organisms present in the upper respiratory tract in health some of them non pathogenic and others *potentially* pathogenic They include various pneumococci α haemolytic and non haemolytic streptococci neisseriae diphtheroids and *H influenzae* Their presence therefore is of no diagnostic significance but repeated isolation of a potential pathogen in predominant numbers correlated with clinical signs often yields strong presumptive evidence on which treatment can be based

The cellular content of sputum is also important Non infective purulent sputum containing large numbers of eosinophils occurs in some asthmatics and a diagnosis of carcinoma of the bronchus can sometimes be confirmed by finding malignant cells in a fresh specimen of sputum

Examination of Pleural Fluid

The character of the fluid may be serous purulent haemorrhagic or chylous Transudates are usually serous with a low specific gravity (less than 1·015) and a low protein content Inflammatory effusions on the other hand are either serous or purulent with a high protein content Bacteriological examination, as for sputum may reveal the causal organism to be the tubercle bacillus or one of the pyogenic cocci The cellular content is also significant consisting mainly of lymphocytes in the common tuberculous effusion (but sometimes polymorphs) neutrophils in pyogenic infections and occasionally eosinophils predominate Red cells are present in large numbers in the blood stained effusions associated with malignant disease and cancer cells can also often be identified by the expert

Skin Sensitivity Tests

Hypersensitivity of the individual to specific foreign proteins can be tested by intradermal inoculation with small doses of suspected allergen The most important skin test is the tuberculin reaction which is discussed at length in a later section Allergy to various pollens is present in hay fever and asthmatics may show hypersensitivity to a wide variety of foreign proteins The Casoni test for hydatid disease is required on occasions to elucidate the nature of a pulmonary cyst and specific tests are also available for certain fungal infections

Assessment of Respiratory Function

With the exception of the residual air subdivisions of the lung volumes can be measured with a simple spirometer and by means of suitable catheters the function of each lung can be assessed separately (bronchospirometry) More complicated techniques are available to assess the ventilation of the lungs the diffusion of oxygen and carbon dioxide the pulmonary blood flow and the actual work involved in breathing

Diseases of the Upper Respiratory Tract

Diseases of the Nose and Nasal Sinuses

The Common Cold (Coryza)

The familiar head cold is an acute catarrhal inflammation of the nose and nasopharynx due initially to a filter passing virus and is spread by droplet infection It occurs in all parts of the world but is most prevalent in temperate zones Although trivial in most cases it is a social menace causing a loss to industry of a tremendous number of working man hours each year In young infants in the elderly and in patients predisposed to bronchitis it is more serious because of its complications Cold and damp seem to predispose to it but exposure to infection is essential Local epidemics are therefor encouraged by crowded public transport attendance at cinemas and other social functions

Clinical Picture The onset is usually rapid with nasal irritation and sneezing slight sore throat, and a clear nasal discharge General symptoms include malaise headache hyperaesthesia of the face and scalp chilliness and slight fever The nose feels congested the airway obstructed and smell and taste may be impaired The acute stage may subside

UPPER RESPIRATORY TRACT INFECTIONS*

Pharyngo-tonsillitis (Sore Throat)

Definition Inflammation of the oro and naso pharynx including the tonsils

Aetiology Most sore throats are due to infection but occasionally to excessive smoking or irritant fumes Known infective agents include viruses and various cocci particularly haemolytic streptococci but in many cases no single organism can be incriminated It is probable that many organisms may be responsible either singly or as a mixed infection and even laboratory investigation can establish the aetiology in only about half the cases Sporadic cases are extremely common localized outbreaks often occur and more widespread epidemics are not infrequent Spread is usually by droplet infection but outbreaks of haemolytic streptococcal infections have been traced to water and milk contamination

Clinical Picture In the milder cases a sore throat develops in a few hours with pain on swallowing general malaise and slight fever The throat feels raw there is a dry painful cough and the mucous membrane over the tonsils palate and pharynx is infected In many cases such symptoms mark the onset of a cold In others they are the prelude to influenza or one of the acute specific fevers In more acute cases particularly those due to haemolytic streptococci the temperature may reach 103 F or more constitutional symptoms are severe and the cervical lymph nodes become enlarged and tender The tonsils may bear the brunt of the infection becoming considerably enlarged and inflamed with patches of yellowish white exudate at the mouths of the crypts (follicular tonsillitis) The whole mucous membrane over the tonsils palate and pharynx may be oedematous and intensely congested and both talking and swallowing become difficult

Differential Diagnosis In all but the milder cases throat swabs should be examined in the laboratory particularly for β haemolytic streptococci and *C diphtheriae* In diphtheria the exudate and necrotic epithelium form a greyish white membrane over the tonsils sometimes extending to the fauces and palate it is not readily detachable A similar appearance may rarely be produced by pneumococcal and staphylococcal infections and in any doubtful case diphtheria antitoxin should be given forthwith without waiting for the throat swab result Other causes of ulceration of the throat, such as Vincent s angina agranulocytosis infectious mononucleosis and acute leukaemia are differentiated by the results of the throat swab and blood count

Course and Complications In mild cases symptoms subside in a few days and clear within a week The acute infections may take longer and complications are more common Infection may spread outside the tonsil to produce a peritonsillar abscess (quinzy) which may require surgical incision Other local complications are otitis media suppuration in the lymph nodes and cellulitis of the neck. Bronchitis and pneumonia may follow by descending infection or aspiration of infected material but they are uncommon particularly in patients receiving chemotherapy The same haemolytic streptococcus may in one patient cause follicular tonsillitis and in another tonsillitis with one or other of the toxic skin erythemas and in yet another the typical picture of scarlet fever A focal nephritis may occur at the height of the infection and the more serious glomerulotubular nephritis may develop 10–21 days from the onset Rheumatic fever may appear after a similar interval Chronic tonsillitis often with enlarged adenoids may follow repeated sore throats

Treatment. The patient should remain at home and severe cases should be isolated and at rest in bed Liberal hot drinks should be taken and the diet should be soft and easily swallowed Many cases require only symptomatic treatment as for a cold with aspirin compounds steam inhalations and a sedative cough linctus Linctus Codeinae 4–8 ml is suitable for an adult and Linctus Simplex 4–8 ml for a child A glycerine and blackcurrant lozenge or any warm syrupy drink is often equally effective in relieving the tickling cough but antiseptic lozenges and gargles have little to commend them

The more severe cases especially those due to haemolytic streptococcal infection should receive chemotherapy with sulphonamides or penicillin Sulphadimidine is safe and reliable an initial dose of 2–4 g followed by 1 g 6-hourly for 2 days then 1 g 8 hourly for 3 days is usually adequate and does much to prevent complications A sulphonamide or penicillin should always be given if the subject is a rheumatic child to prevent relapse and there is evidence also of their value when given prophylactically to check epidemics in closed communities

The decision to remove chronically enlarged tonsils and hypertrophic adenoids is fraught with difficulty but the main indications are frequent attacks of acute tonsillitis recurrent otitis media and hypertrophy of such degree as to interfere with the airway

Infl e a is considered under the infectious diseases (*s e* page 88)

fied or because the patient may seem to be allergic to many foreign proteins

Hay Fever

Definition A paroxysmal and seasonal oedema and congestion of the nasal and conjunctival mucous membranes due to hypersensitivity to various pollens

Aetiology The allergen may be pollen from trees flowers or grasses but in Britain is usually the dry pollen of Timothy grass which is prevalent in the atmosphere during May, June, and July

Pathology The nasal mucous membrane is swollen soggy, and flesh pink in colour due to vaso dilatation and oedema The airway may be com pletely occluded Eosinophils are increased in the blood and are also present in the excessive nasal discharge

Clinical Picture Symptoms usually appear in adolescence and recur each year from May to July or August There is an abrupt onset with fre quent sneezing nasal irritation and obstruction and a profuse watery discharge Conjunctival injec tion, excessive lachrymation and photophobia are frequently present and some general malaise head ache and depression accompany severe attacks Visits to the country are often intolerable particu larly during hay making

Differential Diagnosis The seasonal incidence usually leaves no doubt as to diagnosis and a family history of hay fever or other allergic disorder supports it. Sensitivity to pollen can be confirmed by skin inoculation or scarification through dilute solu tions of the common pollens a distinct wheal and flare appearing within 15 minutes of the injection Coryza is common in the winter months and is further distinguished by its less frequent recurrence clinical course and infectious nature Local causes of nasal obstruction such as a deflected septum polypi etc are excluded by careful examination through a nasal speculum Vasomotor rhinitis is in distinguishable from hay fever except by its occur rence at any time of the year

Course and Complications Attacks usually cease during July or August but return each spring for many years and often for life but in some patients gradually lessen in severity or cease altogether A small percentage become asthmatic in addition and in long standing cases nasal polypi may develop and require surgical removal

Treatment 1 *Preventive* the attacks are less fre quent in towns at the seaside or at sea but the avoidance of pollen altogether is impracticable Specific desensitization although tedious is avail able but should be reserved for those patients who cannot be relieved by palliative treatment Inocula tion should begin in February or three months before symptoms are expected with a small dose of pollen extract e g 5–10 units a syringe contain ing ½ ml of adrenaline should be at hand on each occasion for immediate injection in the event of severe local or general reaction Inoculations are continued every few days with gradually increasing doses, aiming at a tolerance to 50 000 or 100 000 units before the hay fever season Complete or par tial freedom from attacks may be achieved but the duration of the immunity is disappointingly short and the course may have to be repeated each year

2 *Palliative* symptoms can be controlled in the majority of sufferers by one or other of the anti histamine drugs provided they can be tolerated in sufficient dosage without producing undue drows ness Several are available and the most suitable must be found by trial and error Examples are diphenhydramine hydrochloride (Benadryl) 50 mg mepyramine maleate (Anthisan) 100 mg prometha zine hydrochloride (Phenergan) 25 mg and Dibistin (Antistin 50 mg + Pyribenzamine 25 mg per tablet) the total dose being adjusted for each patient Ephedrine 30 mg (½ gr) t d s is effective for short periods and can be taken with an antihista mine Local treatment to the nose is useful particu larly for patients unable to tolerate the drugs by mouth Oily preparations should not be used Nasal drops of or a nebulizer containing ephedrine ½–1 per cent in normal saline or Antistin Privine (Ciba) are suitable Insufflations of hydrocortisone up to 15 mg in 24 hours are very effective in some cases The results of zinc ionization are too un reliable for it to be generally recommended

Perennial Allergic Rhinitis (Vasomotor Rhinitis)

This condition resembles hay fever closely but is not seasonal and occurs at all times of the year The eyes are less affected than in hay fever but the nasal symptoms and pathological changes in the nasal mucous membrane are essentially the same Inhaled allergens thought to be responsible include pollens house dust animal dander face powder containing orris root moulds feathers kapok and bacteria A single causal factor is seldom found the patient often showing multiple hypersensitivity

Treatment If a causal agent is identified it should be avoided where possible Desensitization seldom yields lasting results Symptoms are often aggra vated by dusty and hot, stuffy atmospheres and the bedroom should be cool and as free from dust as possible (*see under* Asthma) Cold bathing of the face or a stroll in the cool of the evening before retiring will often bring relief for some hours and prevent disturbed sleep Symptomatic treatment is the same as for hay fever

pletely as possible Avoidance of any causal or aggravating factors discovered in the history is essential if relapse is to be prevented Smoking should be discouraged and education in voice production may be necessary where the occupation makes undue demands upon the voice Nasal and oral sepsis should be treated Local applications to the larynx are of doubtful benefit but some symptomatic relief is given by a menthol lozenge containing 30 mg (½ gr) of menthol

Diseases of the Lower Respiratory Tract

Acute Tracheo-bronchitis

Definition An acute inflammation of the mucous membrane of the trachea and bronchi

Aetiology Most cases are due to infection which not infrequently begins in the upper respiratory tract and descends to affect the tracheo bronchial tree Thus it often occurs with coryza influenza or any of the ill-defined group of febrile catarrhs which affect the upper respiratory tract It is probable that viruses are the initial invaders and that the common organisms found in the sputum *i e Strep viridans M catarrhalis H influenzae* and various pneumococci play only a secondary rôle Specific infections in which an acute bronchitis may occur include measles whooping cough smallpox and typhoid fever An acute chemical bronchitis follows exposure to certain vapours and fumes particularly irritant being ammonia chlorine oxides of sulphur and nitrogen and the war gases lewisite and mustard gas

Predisposing Factors. It occurs particularly in cold damp foggy weather so that the maximum incidence is during the winter months Infants and elderly people are more susceptible as are also patients with chronic pulmonary diseases or pulmonary congestion due to mitral stenosis or chronic left heart failure A constitutional factor may also be suspected in patients who develop it with every cold and there is sometimes a familial tendency Heavy smoking dusty occupations and the inhalation of irritant fumes may also predispose to an acute attack but they are of greater importance in recurrent and chronic bronchitis

Pathology Initially there is congestion and oedema of the mucous membrane of the trachea and main bronchi Secretion is scanty at first but increases in a few days gradually becoming mucopurulent or purulent according to the type and degree of secondary infection There is some epithelial desquamation and in severe cases the changes extend down to the bronchioles causing obstruction to the lumen with patchy lobular atelectasis or pneumonia distally

Clinical Picture Symptoms of tracheo bronchitis often preceded for a day or two by those of nasopharyngitis or laryngitis begin with soreness down the trachea and a raw feeling behind the sternum A frequent dry and painful cough develops sometimes causing the patient to clutch his neck in his efforts to suppress it General tightness across the upper chest and a sense of wheezing not amounting to true dyspnoea are common complaints Moderate fever to 100–103 F and general malaise are usual For a few days the cough produces only a little viscid mucoid secretion the sputum then becomes more profuse mucopurulent and easily expectorated and at this stage the cough ceases to be painful and the general symptoms begin to subside The average case recovers in 7–10 days although cough and sputum may persist but gradually diminishing over a further week or two The severity of the attack however depends upon how far down the bronchial tree the infection extends should it reach the bronchioles the more serious condition of capillary bronchitis or bronchiolitis results This is often clinically indistinguishable from broncho pneumonia the general symptoms being more severe dyspnoea and cyanosis becoming apparent and recovery is correspondingly slower

Examination of the chest reveals no abnormality if the trachea alone is involved When the larger bronchi are affected rhonchial fremitus may be detected and sonorous rhonchi varying with cough may be heard Coarse rales and mucous clicks appear as bronchial secretion increases When the whole bronchial tree is involved generalized rhonchi of all pitches are audible both in inspiration and expiration and are accompanied by rales as the sputum increases Radiological examination is normal in the uncomplicated case except for some intensification of the normal broncho vascular pattern

Differential Diagnosis From the history and clinical features diagnosis is usually straightforward In young children the specific fevers should be borne in mind particularly measles and a search made for Koplik s spots Altered breath sounds and percussion note are an indication for advising a radiograph of the chest as is also the persistence of symptoms beyond a fortnight

Complications Aspiration pneumonia (*see* p 337)

Laryngitis

Acute Laryngitis

Inflammation of the laryngeal mucosa may follow or accompany any infection of the upper respiratory tract or bronchi Most commonly it develops with or as a sequel to the common cold but it may also be a feature of other virus infections including measles and influenza It may also follow local trauma from excessive smoking irritant gases hot steam instrumentation and abuse of the voice

Pathology The mucosa is congested and slightly swollen particularly over the vocal cords with an excessive mucous secretion The epiglottis and aryepiglottic folds are also frequently involved and severe cases show oedema with considerable narrowing of the lumen

Clinical Picture The general features are similar to those of coryza with the addition of hoarseness of the voice or even aphonia Talking and swallowing may be painful and the larynx itself tender to external palpation The cough is at first frequent dry and painful but in a few days becomes painless and productive of mucoid or mucopurulent sputum Symptoms usually subside in 7–14 days but in some patients roughness of the voice and cough may persist for a few weeks

Complications The infection may descend the bronchial tree causing tracheo bronchitis or pneumonia Particularly in infants where the laryngeal aperture is already small attacks of laryngeal spasm may occur with stridor acute dyspnoea cyanosis and sometimes loss of consciousness (laryngitis stridulosa or croup) These attacks are commonest at night With loss of consciousness the spasm relaxes breathing is resumed and recovery ensues The most serious complication of acute laryngitis is oedema of the larynx of sufficient degree to cause complete obstruction

Differential Diagnosis This includes all forms of hoarseness and aphonia (*see under* Chronic Laryngitis)

Treatment Treatment is essentially the same as for a severe cold but the course of the illness is longer full recovery often taking 2–3 weeks Rest in a warm room is advisable and bed rest during the first few days if the patient is febrile Smoking is better avoided and talking should also be discouraged Steam inhalations are soothing and may be given for 5–10 min 3 or 4 times daily Children too young to use inhalations can be nursed in a steam tent Medicated steam has no great advantage in the early days and frequently causes unnecessary coughing The initial unproductive cough can be suppressed by a sedative linctus such as Linct Codein or Linct Methadoni 4 ml (1 teaspoonful) or a pill such as Tab Cod Phosph 30-60 mg (½–1 gr) When the cough begins to loosen expectoration can be assisted by substituting Vap Menthol et Benzoin for the plain steam and a simple expectorant mixture may also help An antibiotic is not generally indicated but should be given to young infants and the elderly in view of the greater risk of descending infection Oral penicillin 125–250 mg 4 hourly is suitable for an adult

Laryngitis stridulosa is usually relieved by a steam tent but a sedative at night may be required to prevent the attacks Chloral hydrate 0 2 g (3 gr) is suitable for an infant aged 1 year Impending laryngeal obstruction is heralded by severe dyspnoea stridor cyanosis and vigorous inspiratory efforts Oxygen should be administered and the larynx should be sprayed with 1 100 adrenaline solution Preparation should be made for tracheotomy in case the obstruction becomes complete

Chronic Laryngitis

Chronic or persistent laryngitis may follow recurrent acute laryngitis It may arise from continued and excessive use of the voice as in bookmakers auctioneers clergymen and untrained singers especially if the occupation is resumed before recovery from an acute attack is complete Heavy smoking alcoholism and dust laden atmospheres also predispose to it and in a few cases chronic sinus infection is responsible Specific forms of chronic laryngitis with ulceration of the mucosa are caused by tuberculosis and less commonly by syphilis

Pathology The vocal cords and laryngeal mucosa are usually thickened and irregularly hyperaemic but in long standing cases the mucosa may be atrophic Cord movements are sluggish but full Ulceration is uncommon except in the tuberculous type

Clinical Picture Men are more commonly affected than women the presenting symptom being a persistent weakness or hoarseness of the voice Efforts at phonation are forced but produce only a harsh or croaking voice A frequent desire to clear the throat and an irritating cough produce only a little viscid mucus (Tuberculous laryngitis is discussed on p 356)

Differential Diagnosis The diagnosis is made on the history by enquiry into the predisposing factors and by inspection of the larynx The latter is essential to exclude the many other causes of hoarseness including benign and malignant neoplasms foreign bodies and the various forms of vocal cord paralysis

Treatment The voice should be rested as com

The treatment is the same as for acute bronchitis and potassium iodide 0 3–1 g (5–15 gr) t d s is thought to encourage early separation of the casts

Chronic Bronchitis

Definition Chronic inflammation of the bronchial mucosa associated with excessive secretion of mucus from the bronchial glands

Aetiology In many cases the disease seems to date from an acute attack of bronchitis but many factors other than infection play a part in its causation and aggravation It is more frequent in cold damp foggy regions than in warm dry and dust free areas Men are affected more than women the commonest age of onset being 50 years and over but no age is immune Inhabitants of industrial towns suffer to a greater extent than country dwellers possibly owing to the effects of air pollution particularly by the oxides of sulphur Dusty occupations also predispose to it as do smoking heavy alcohol consumption and obesity The incidence also bears some relation to social class as it is maximal in the lower income groups Chronic sepsis in the upper respiratory tract and around the teeth may be factors in its persistence but are seldom causal Many of the factors believed to play a part in the development and persistence of this disease do so by chronic bronchial irritation but in a proportion of cases no obvious irritant can be indicted and a constitutional factor is thought to be responsible particularly when there is a family history of the disease in near relatives

Pathology In the early stages there is hypertrophy of the mucous glands and an increase in the number of goblet cells The mucosa and submucosa are oedematous and infiltrated with lymphocytes and in some areas the epithelium undergoes metaplasia In established cases the changes extend down to the bronchioles the lumen becomes blocked with infected secretion and distal to this obstruction a variety of pathological changes can be seen including simple atelectasis miliary abscesses or pneumonia and fibrosis Surrounding alveoli undergo compensatory emphysema and in long standing cases patchy areas of bronchiectasis are frequently found

The organisms found in the sputum are those normally confined to the upper respiratory tract but pneumococci and *H influenzae* are commonly present in increased numbers and are the commonest bacteria isolated during exacerbations of the disease

Clinical Picture There may be a history of recurrent catarrhal infections or asthma in childhood or the patient may date his symptoms accurately from an attack of pneumonia or acute bronchitis Most commonly however symptoms begin in the winter months with a cold which goes down to the chest and takes some time to resolve It recurs each winter for a few years taking rather longer each time for the cough and wheeziness to subside Eventually cough and sputum persist into and through the summer months and are accompanied by progressive dyspnoea Each winter exacerbation sees an increase in the amount of sputum which changes from scanty viscid mucus to more profuse mucopus Occasional cases are seen in which the sputum consists of several ounces of serous frothy fluid daily (bronchorrhoea serosa) Symptoms may have been present for many years before medical advice is sought the patient dismissing his chronic cough as due to smoking Occasional slight blood staining or flecking of the sputum is quite common but frank haemoptysis is rare Localized chest pain is not a feature of uncomplicated cases but a general tightness across the chest is a very common symptom It may be most noticeable on exertion but advanced cases often experience attacks of coughing and bronchospasm in the early hours of the morning very similar to spasmodic asthma

Examination of the chest usually reveals rhonchi of all pitches over both lungs with prolonged expiration The rhonchi may clear temporarily on coughing In time signs of emphysema also become apparent Clubbing is not a feature of the uncomplicated case Persistent râles suggest patchy areas of pneumonia or atelectasis if heard during an acute episode and bronchiectasis if present between exacerbations

Radiological examination in the early stages shows no abnormality except perhaps some increase in the broncho vascular striations During acute exacerbations areas of segmental or sub segmental atelectasis are not infrequent Bronchography may show irregularities of the bronchi with some widening of the lumen and dilated mucous glands appearing as diverticula in the bronchial walls There is frequently evidence of emphysema in addition

Diagnosis The long history and clinical examination usually suggest the diagnosis but other causes of chronic cough must be considered Chronic pulmonary tuberculosis is excluded by radiography of the chest and examination of the sputum for tubercle bacilli Bronchiectasis should be suspected if there is clubbing of the fingers (*see* Plate 16 1) persistent purulent sputum and localized basal râles between exacerbations Chronic left ventricular failure or the pulmonary congestion associated with mitral stenosis may closely mimic chronic bronchitis but careful clinical examination should avoid

or a specific bacterial pneumonia are the commonest complications, particularly at the extremes of age and are frequently heralded by the development of pleurisy Temporary aggravation of symptoms is common in asthmatics and in patients with bronchiectasis Patients with chronic pulmonary tuberculosis may suffer an exacerbation of symptoms due to the secondary infection with an increase also in the abnormal X ray shadows which may be slow to resolve Cor pulmonale may be precipitated in patients with extensive pulmonary disease particularly emphysema and cardiac failure in those with pre-existing heart disease Inadequate treatment and convalescence are factors in paving the way for chronic bronchitis

Treatment *General Régime* Rest in bed in the orthopnoeic position until the temperature has been normal for 2 or 3 days is advisable The room should be well ventilated but free from draughts and the temperature maintained around 65 F Humidifying the atmosphere by steam kettle or steam tent eases the cough and loosens the sputum Diet can be dictated by taste and appetite but frequent hot drinks should be encouraged to a minimum of 4 pints daily

Specific Treatment The uncomplicated mild case does not benefit from chemotherapy and recovers without it However in elderly subjects and young infants in patients subject to recurrent bronchitis in those with chronic lung disease, or in the more seriously ill cases where pneumonia is a definite risk an antibiotic should be given The choice may be determined by the bacteriology of the sputum but in general a broad spectrum antibiotic *e g* tetracycline is recommended It is given orally in doses of 0 5 g 6-hourly for 2–3 days followed by 0 5 g t d s for a further 2–3 days Oxygen should be administered for cyanosis and specific treatment for cardiac failure may also be required

Symptomatic Treatment The painful unproductive cough in the early stages can be relieved by steam inhalations Smoking should be avoided Further suppression of the cough is achieved by Linct. Codein or Linct. Methadoni 4 ml (1 tea spoonful) 3 or 4 times a day and the tightness in the chest can be partly relieved by ephedrine 30 mg (½ gr) t.d s An aspirin mixture may be required for the general symptoms and an hypnotic to secure adequate sleep Morphine compounds and barbiturates should be avoided for this purpose if there is any tendency to cyanosis or much bronchial secretion but choral hydrate 1–2 g (15–30 gr) or paraldehyde 4–8 ml can be used with safety As soon as the cough loosens the linctus should be replaced during the day by an expectorant mixture The time honoured Mist Sod Chlorid Co (N F) ½ oz in hot water t d s is quite effective the first dose to be taken on waking If this causes vomiting Mist Pot. Iod Ammon (N F) ½ fl. oz t d s can be given instead Postural drainage for the lower lobes morning and evening should be instituted where there is much sputum

Recovery should be followed by a convalescent holiday away from the polluted atmosphere of the towns and work should not be resumed until all symptoms and signs have cleared

Special Varieties of Bronchitis

Acute Laryngo-tracheo-bronchitis of Infants

This is distinguished by the severity of the illness and signs of laryngeal or tracheal obstruction The child rapidly becomes acutely ill pale and cyanosed, with evidence of respiratory obstruction in addition to the general signs of bronchitis Stridor is evident. The accessory muscles of respiration are seen in action and the intercostal spaces are drawn in with each exaggerated inspiratory effort

This is a medical emergency and the child should be treated in hospital It should be nursed in a steam tent and tetracycline should be given at the onset in the full dose for the child s age To improve the airway viscid sputum may be removed by suction through a rubber catheter if necessary at bronchoscopy, and preparations should be made for tracheotomy which should not be delayed if the child shows signs of collapse

Plastic or Fibrinous Bronchitis

This is an uncommon form of acute bronchitis in which casts of the bronchial tree are expectorated It is probably not a specific disease, as bronchial casts are occasionally coughed up by patients with asthma or during exacerbations of chronic bronchitis Other cases however occur in patients with no previous chest illness the onset being indistinguishable from acute catarrhal bronchitis Symptoms increase with dyspnoea cyanosis and spasms of coughing in which the casts are expectorated Pulmonary atelectasis and respiratory obstruction are occasional complications which may necessitate bronchoscopic aspiration The casts consist largely of mucus with a little fibrin and they decrease in size as the illness runs its course until several fine casts corresponding to the smaller bronchi are produced each day Large casts are usually hollow and the smaller ones solid

The signs are those of bronchitis with periods of partial respiratory obstruction during separation of a large cast. A flapping sound (bruit de drapeau) may be audible at this time and areas of atelectasis may be detected

hood or before the age of twenty An intractable form is not uncommon in middle life especially in women just after the menopause and in those subject to bronchitis

Predisposing and Exciting Factors *Heredity* The family history often reveals cases of asthma or other allergic disorder in other members of the family and the view is widely held that a constitutional factor may be responsible for the hypersensitivity of the bronchial tree to a variety of extrinsic irritants or internal stimuli

Allergy Allergy plays an important role in asthma and the hypersensitivity is usually to a foreign protein substance Even minute doses of the offending allergen quite innocuous to normal individuals may precipitate an attack in a sensitized person Other allergic disorders *e g* hay fever urticaria eczema are not uncommonly encountered in the same patient Inhaled allergens commonly responsible are certain dusts including house dust grass tree and flower pollens orris root powder feathers and animal dander and possibly bacteria Ingested allergens include milk eggs chocolate wheat flour shell fish and strawberries It is however comparatively seldom that a patient or his doctor can identify a single allergen The attempt should be made since its avoidance may bring prolonged relief from attacks Even so disappointment may follow since the fundamental defect in many asthmatics seems to be their capacity to acquire hypersensitivity to various protein substances rather than a fixed allergy to one or more An idiosyncrasy to certain drugs is an occasional cause the most frequent being aspirin It is remarkable that a small dose of aspirin in such patients may precipitate a severe paroxysm whereas other asthmatics find aspirin an effective remedy

Occupational Hazards A proportion of workers exposed for some years to cotton dust develop a form of asthma and bronchitis (byssinosis *see* page 380) in which the symptoms characteristically are worst on Monday mornings and lessen as the week progresses A specific form of asthma with nasal irritation and sneezing is also found among those in contact with platinum salts Apart from the few specific causes however any dusty occupation may aggravate the condition

Reflex Causes It is by no means clear what part reflex vagal stimulation plays in asthma but such reflexes are postulated in cases which seem to be precipitated by exertion exposure to cold air dyspepsia or infection of the respiratory tract

Climate Asthma occurs in all countries but since it is aggravated by repeated respiratory tract infections the sufferer is usually better in a warm dry climate At an altitude of 4 000 ft attacks may cease possibly as a result of the low dust and bacterial content of the atmosphere and the same freedom from attacks may be experienced at sea

Endocrine Factors In some women attacks occur only with menstruation or during the week before and they may cease with the menopause To regard such cases as of emotional origin fails to explain the pre menstrual attacks which sometimes occur in patients with irregular periods and who have no other symptoms of pre menstrual tension Attacks not infrequently cease during pregnancy and some children grow out of it at puberty

Emotional Factors In general the asthmatic is emotionally less stable and more prone to mental tension than the average Prolonged anxiety or an acute psychological trauma tends to aggravate the condition and may induce status asthmaticus Children are particularly susceptible to an atmosphere of conflict or nervous strain and attacks may cease only when they are removed from the influence of over anxious parents Long standing cases may become introspective irritable and rather selfish these emotional traits being often the consequence rather than the cause of their disability

Pathology During the attack there is vascular engorgement and oedema of the bronchial mucosa and spasm of the bronchial musculature Eosinophilia may be present in the blood and in the sputum which sometimes contains Curschman s spirals and Charcot Leyden crystals In fatal cases the lungs are over inflated the bronchioles are obstructed by viscid mucus and shed bronchial epithelium and their walls congested and infiltrated with eosinophils Evidence of bronchitis patchy atelectasis or broncho pneumonia may also be found

Clinical Picture The severity and duration of the paroxysms vary enormously from slight wheezing for a few minutes to intense dyspnoea for several days The average attack lasts an hour or so and commonly disturbs a patient from sleep in the early hours of the morning It may however occur at any time and the first symptom is a sense of tightness or constriction in the chest This increases rapidly to extreme dyspnoea with wheezing particularly on expiration The patient sits upright or leans forward with hands on knees fighting for breath and using all his accessory muscles of respiration The chest is distended the shoulders hunched inspiration consists of short gasps through the open mouth and each is followed by a prolonged and laboured expiration the cervical veins become distended and cyanosis is often present Breathing is further embarrassed by the frequent short ineffectual cough and the terror which the feeling of suffocation engenders After a variable period the attack begins to subside gradually The

error Bronchial carcinoma must also be considered when the history is comparatively short

Course and Complications Cough Syncope During a bout of coughing the victim may suddenly lose consciousness and fall to the ground The attack is due to diminished venous return and consequent fall in cardiac output and blood pressure brought about by the raised intrathoracic pressure during violent coughing Attacks of pneumonia are more frequent in subjects with this disease particularly during the winter months and may cause death If the condition cannot be relieved emphysema develops in the course of time and after some years the final scene closes with respiratory insufficiency or cardiac failure

Treatment *Preventive* There is much scope for preventive measures to combat this common and crippling disease which in this country takes a large toll of human life and suffering mainly in the lower social classes and especially in the industrial towns and cities Improvements in housing education and working conditions must continue and the national problem of smoke abatement must receive urgent attention before any great reduction in the number of victims can be expected

While the patient is still at the stage of recurrent bronchitis advice and strict treatment are often rewarding Any patient with an acute respiratory infection in whom cough and sputum persist and are accompanied by a wheezy type of dyspnoea should have a full convalescence if possible out of town in the country or at the seaside If the condition tends to recur each winter or with each cold the occupation and place of residence should be carefully reviewed in order to detect and remove if possible any form of bronchial irritation Smoking should be firmly discouraged and the doctor must not be persuaded by the patient that his first cigarette helps him to cut the phlegm it does so but only by making him cough more vigorously and by bronchial irritation promoting a further flow of mucus There is a place for the prophylactic use of antibiotics but it is not always effective and the hazards of drug resistance and toxic effects are considerable It should never be employed to the neglect of the other preventive measures and should be reserved for the severe cases Tetracycline 250 mg t. or q d s gives fairly reliable results if well tolerated and can be given throughout the winter months or at times of increased susceptibility e g at the first sign of a cold or during foggy weather

Symptomatic and Curative Treatment of the established case is often disappointing Acute exacerbations may be avoided if the patient can spend the winter months in a warm dry climate but for the majority this luxury is impracticable and they should be advised to live away from industrial areas if possible Patients compelled by circumstances to remain in the cities should avoid as far as possible the smoke laden, infectious atmospheres of public houses cinemas and public transport and should remain indoors during fogs Even mild cases should give up smoking

Symptomatic treatment is a distinct help A suitable expectorant should be found for each individual by trial and error Mist Pot Iod Ammon (N F) or Mist Sod Chlorid Co (N F) taken in hot water will be found as useful as any When there is much sputum postural drainage for the lower lobes (*see* under Physiotherapy in Diseases of the Chest p 384) should be practised for 15 min each morning and evening Anti spasmodics taken regularly afford considerable relief the most useful for continued use being ephedrine 30–60 mg (½–1 gr) t d s or Isoprenaline 10–20 mg sublingually The dose should be increased gradually up to the limit of tolerance for each patient As an alternative choline theophyllinate 200–400 mg t or q d s may be tried If bronchospasm is severe a more rapid effect is provided by inhaling a mist of Neb Adrenal et Atrop Co or similar solution from a hand atomizer As long term therapy a course in general relaxation and deflation breathing exercises is well worth while as it improves the patient's exercise tolerance enables him to recover more rapidly from dyspnoea and may possibly delay the progress of the secondary emphysema

During acute episodes the regime is the same as for acute bronchitis and antibiotics should be given in full dosage Penicillin alone although effective in many cases is not the best choice as *H influenzae* is insensitive to it and if this organism is present in the sputum an early relapse is common Streptomycin 1 g i m b d should be given in addition or alternatively a course of one of the tetracyclines Postural drainage should be intensified during such times and expectoration can be further assisted by detergent aerosols Appropriate treatment for cardiac failure and respiratory insufficiency may also be required

Bronchial Asthma

Definition A syndrome characterized by attacks of wheezy dyspnoea due initially to spasm of the muscle in the bronchial walls Mucosal engorgement and hypersecretion of mucus accompany the paroxysm and increase the difficulty in breathing which is mainly in expiration

Aetiology Many factors are concerned in the aetiology of asthma and it is seldom that a single agent can be identified The disease may begin at any time of life in either sex but generally in child



Lobar Pneumonia (R U L)

cough loosens and following the expectoration of small amounts of tenacious mucus expiration be comes more free and relaxed the patient lies back exhausted and frequently falls to sleep from which he may awaken free of any symptoms or signs of his recent distress

Examination of the chest during an attack reveals the over inflation and impaired excursion of the thorax and diaphragm The percussion note is hyper resonant with diminution of cardiac and liver dullnesses and rhonchial fremitus is often detect able The breath sounds are obscured in all areas by rhonchi of varying pitch both in inspiration and expiration the expiratory phase being greatly pro longed. As the attack develops and more mucus is secreted generalized râles are also heard

Between attacks the chest may be quite normal or there may be a persistent slight wheeze In the course of time the chronic sufferer develops chest deformity with raised shoulder girdle dorsal kypho sis and increased antero posterior diameter the lungs showing signs of progressive emphysema

Radiological examination during an attack is usually normal but segmental or lobar atelectasis is occasionally seen It is usually transient but if it does persist may lead to bronchiectasis In a few cases non segmental infiltrative shadows appear from time to time in various parts of the lung fields often bilaterally They are associated with eosinophilia in the blood and a preponderance of eosinophils in the inflammatory exudate This group at present ill defined is referred to as pulmonary eosinophilia

Complications During an acute episode pul monary atelectasis of varying extent or spontane ous pneumothorax is occasionally discovered In chronic cases the passage of time sees the develop ment of emphysema with progressive diminution in pulmonary function Long standing cases usually show the clinical signs of chronic bronchitis (asth matic bronchitis ') and are indistinguishable from cases of chronic bronchitis with intermittent exacer bations of bronchospasm (bronchitic asthma) Prolonged severe asthma or status asthmaticus may cause death from asphyxia

Differential Diagnosis Organic bronchial obstruc tion must be excluded particularly if it is the first attack Foreign bodies in children and tuberculous strictures or neoplastic obstruction in adults may cause a wheeze which is unilateral and often localized A chest radiograph should always be taken in such cases and bronchoscopy be performed in cases of doubt

Emotional Dyspnoea only one manifestation of a general anxiety state is usually easy to recognize The patient complains that he cannot get enough air into his lungs and will be seen to sigh fre quently and deeply during the examination, which reveals no evidence of bronchospasm or other pul monary abnormality

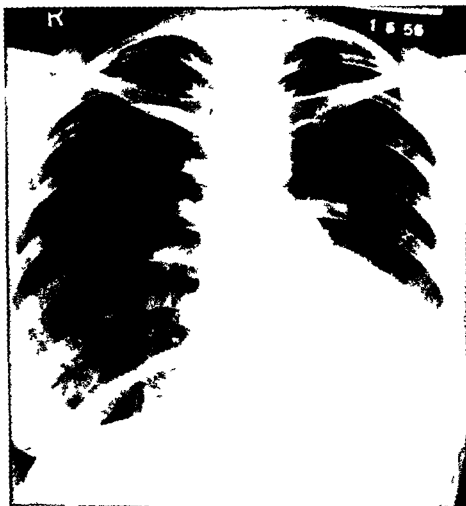
Hyperventilation attacks occur in the hysterical personality Respiration is increased both in rate and depth presumably in response to subconscious impulses initiated by anxiety or fear The excessive excretion of carbon dioxide causes respiratory alkalosis which is attended by unpleasant sensations of giddiness palpitations clouding but not loss of consciousness tingling of the extremities and some times tetany There is no evidence of bronchospasm and demonstration of the cause of the symptoms by instructing the patient to over breathe for a few minutes will often prevent their recurrence If in sight is lacking the patient should be advised to hold the breath at the first sign of an attack or to breathe in and out of a paper bag in order to retain carbon dioxide

Differentiation from paroxysmal nocturnal dys pnoea (cardiac asthma ') is most important since adrenaline is contra indicated in this condition and morphine the essential treatment of cardiac asthma should on no account be given in an asthmatic attack So called cardiac asthma is due to pulmo nary congestion and oedema and is usually a sign of left ventricular failure There is nearly always evidence of left ventricular enlargement due most commonly to hypertension but in younger subjects to aortic valve disease Other signs of value include an apical triple rhythm and pulsus alternans Similar attacks occur in severe mitral stenosis and the characteristic signs must be sought in all cases of doubt Although there may be some evidence of bronchospasm the main pulmonary signs in cardiac asthma are generalized rales and the patient may expectorate a considerable quantity of blood stained frothy sputum

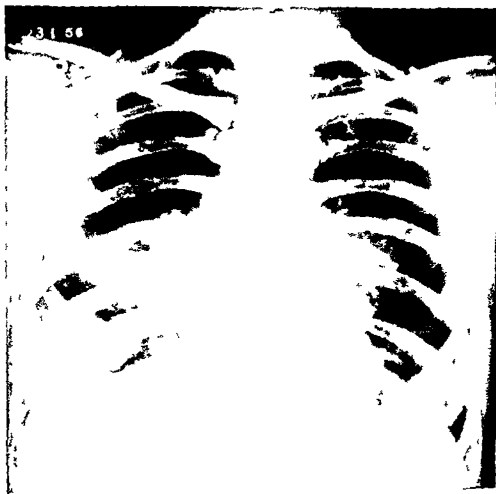
The relationship of simple asthma to the group of conditions referred to as pulmonary eosino philia is not yet established This group includes Loeffler s syndrome asthma with eosinophilic pul monary infiltrations tropical eosinophilia and some cases of periarteritis nodosa In any of these the presenting clinical feature may be asthma

Treatment. The objects of treatment are to relieve the paroxysm as soon as possible and to institute measures to prevent further attacks

Treatment of the Acute Attack The first essential is the administration of a bronchodilator drug the route of administration depending on the severity of the attack A slight attack can often be aborted by ephedrine 30–60 mg (½–1 gr) orally but the main use of this drug is in preventing recurrent attacks Isoprenaline (Neo Epinine) 20 mg sublingually is more effective at the onset than ephedrine since it



TUBERCULOUS LOBAR PNEUMONIA



Viral Pneumonia

acts more quickly For more severe attacks, however the anti spasmodic should be given by injection or inhalation Adrenaline 1 1 000 solution is an effective remedy and 0·3 to 0·6 ml (5–10 minims) should be given subcutaneously early in the attack, care being taken to avoid intravenous injection This dose can be repeated every 15–20 minutes for three or four doses Alternatively a solution of adrenaline 1 100 may be inhaled as a mist from a hand inhaler *It is important to ensure that the apparatus is used* properly and that the patient understands the necessity of squeezing the rubber bulb to coincide with inspiration A few inhalations repeated several times if necessary will be found a rapid and effective remedy and side-effects from this method are less frequent than after subcutaneous injection There are several hand atomizers on the market and several proprietary solutions for use therein In general it will be found that 1 100 adrenaline 1 per cent isoprenaline or Neb Adrenal. et Atrop Co (N F) are quite adequate but some patients prefer a proprietary brand An intelligent patient may be taught to give adrenaline to himself by injection but such patients must be carefully chosen Too often the method is abused, the drug being taken in increasingly large doses and too frequently so that it loses its efficacy the asthma persists but is aggravated by the side-effects of adrenaline *i e* palpitations tremulousness apprehension insomnia and general weakness In such cases or when adrenaline fails the drug of choice is aminophylline (theophylline with ethylene diamine) Ten to 20 ml containing 0·25 to 0·5 g are given slowly intravenously and repeated in two or three hours if necessary Alternatively 0·5 g can be added to a pint of 5 per cent glucose and given by intravenous drip Aminophylline is also fairly effective given rectally as a suppository containing 0·5 g but its effect is delayed Oral preparations are not recommended for any but the mildest attacks as an effective dose is apt to cause gastric irritation and intramuscular injections are too often extremely painful

In addition to a bronchodilator a sedative may be prescribed and caution is necessary in making the choice Morphia is dangerous and should never be given, not only because of the risk of addiction but because a fatal issue may follow from respiratory depression Pethidine should be avoided as it increases the viscosity of the sputum The barbiturates are safe in the absence of cyanosis and amylobarbitone sodium (sodium amytal) 100–300 mg (1½–5 gr) or quinal barbitone sodium (seconal sodium) 50–200 mg (¾–3 gr) are satisfactory Alternatively chloral hydrate 1·0–2·0 g (15–30 gr) by mouth can be recommended

A patient in status asthmaticus should be treated in hospital Often removal from the home atmosphere of panic and despair will initiate an improvement and he may respond to adrenaline or aminophylline in full dose as indicated above soon after admission. The Hurst method of injecting 1 minim of adrenaline 1 1 000 each minute until improvement sets in is often successful but must be used with caution in hypertensive and elderly individuals. Oxygen should be given through a B L B mask plastic envelope or in an oxygen tent and sedation may be achieved with paraldehyde 5–10 ml intramuscularly or twice this dose rectally in 5–6 oz of water Expectoration can be materially assisted by a detergent aerosol such as "Alevaire" from a suitable atomizer attached to an oxygen cylinder An antibiotic should also be given the choice being determined by the bacteriology of the sputum If all these measures fail then steroid therapy is indicated. Adreno-corticotrophic hormone (ACTH) is slightly more effective than cortisone and is given intramuscularly in a dose of 25 mg 6-hourly for 2–3 days the dose being gradually reduced over the next few days to zero Alternatively ACTH 25–50 mg in a litre of 5 per cent glucose can be given daily by intravenous drip ACTH gel 40 units i.m b d is also very effective the dose again being tapered off as improvement occurs *Cortisone is given by mouth in a dose of* 300–500 mg/day for the first day or two followed by 100 mg daily and then 50 mg daily for a few more days Prednisolone (delta hydrocortisone) or triamcinalone may be effective in the smaller dosage of 5–10 mg q d s and side-effects are less common Complete reliance should not be placed on steroid therapy to the exclusion of the measures already outlined since even when successful its effects are not apparent for several hours. Whenever resort is had to these hormones their undesirable effects should be borne in mind

Management Between Attacks The patient whose life is already burdened by asthma should not be rendered more miserable by further restrictions without good reason Constant encouragement to lead as full and natural a life as possible and an optimistic outlook should be maintained Advice must be based on a careful history of each individual but certain general rules apply to most chronic sufferers. Physical and mental fatigue should be avoided as should also extremes of temperature and foggy districts. Diet need not be restricted except on good evidence of a particular allergen, but heavy meals should not be taken late in the evening as gastric distension seems to be a precipitating factor in many patients Bronchial irritation as for a chronic bronchitic should be reduced to a minimum if necessary by change of occupation and by

(a)

(b)

PULMONARY TUBERCULOSIS

(a) Bilateral upper zone infiltration with cavitation on left
(b) Same patient two years later after treatment with chemotherapy and an artificial pneumoperitoneum

PLATE 16.6

symptoms are relieved or to just short of that which *causes side effects of tremor sweating palpitations* and difficulty in starting micturition Patients in tolerant of ephedrine can frequently take isoprena line 10–20 mg sublingually instead but if neither is tolerated in effective dosage choline theophyllinate 200–400 mg t d s may be tried

In many cases potassium iodide 1 g (15 gr) t d s assists in loosening the tenacious mucoid sputum The smaller doses which most stock mixtures con tain are not so effective but if iodism results Mist Sod Chlorid Co (N F) provides an alternative

By combining a suitable antispasmodic with a sedative the asthmatic in whom the element of mental tension seems to be a factor can receive further help and night attacks can often be pre vented in this way There are several convenient combinations of this kind on the market Anti histamines are disappointing but promethazine hydrochloride (Phenergan) 25 mg at night in place of a sedative is effective in some cases

The large number of proprietary remedies avail able for the treatment of asthma is eloquent testi mony to the lack of a specific treatment Most of these contain two or more of the various drugs already mentioned combined in tablet or powder form The physician must guide the patient in his choice after proper trial of the individual constitu ents The inhalation of smoke from asthma cigar ettes and various powders containing stramonium and nitrates should be discouraged as their con tinued use causes further bronchial irritation and *other remedies are more efficient Within reason* however the sufferer should be permitted his favourite preparation and most severe cases choose to carry a hand atomizer Finally in intractable cases with frequently occurring severe attacks treatment with steroid hormones must be considered The results can be quite dramatic but cases must be carefully selected with due regard to the precautions and attendant risks (p 130) They should not be given to patients with peptic ulcer or pulmonary tuberculosis although apparently healed and are best avoided where bronchial infection is a predomi nant factor Intercurrent infections in patients receiving long term steroid therapy must be treated promptly with antibiotics and the increased hazard of injuries and surgical operations must be met by a temporary increase in dose ACTH has to be given by injection Long acting preparations are satisfac tory given once daily intramuscularly beginning with 40 units and adjusting the dose after a few days Cortisone is given by mouth the amount required being usually 50–75 mg daily in divided dos s Better results however with fewer side-effects are usually obtained with prednisolone or triam cinalone Initial control is established with 20–40 mg daily for a few days and the dose then gradually reduced by 5–10 mg every two days until the minimum maintenance dose is discovered This usually lies between 5 and 15 mg daily

Prognosis It is impossible to predict the course of this disease but many patients live a normal span of years in reasonable health in spite of it Children may cease their attacks at puberty and adults often have long periods of freedom Death may occur in status asthmaticus particularly in the long standing victim who has secondary emphysema *and in whom the status has been precipitated by an* acute respiratory infection The same type of patient may also die ultimately of respiratory or cardiac failure

PULMONARY ATELECTASIS (ABSORPTION COLLAPSE)

Definition The word atelectasis literally means failure of *expansion and in its true sense is seen* only in the foetus or in the newborn when part or the whole of the lungs may fail to aerate By common usage however the term is applied to an acquired state of airlessness of previously func tioning lung alveoli This definition excludes the partial collapse of lung with diminution of air content which occurs when the pleural space con tains air or fluid (passive collapse or relaxation collapse) the mechanics of which are quite differ ent

Pathogenesis The fundamental cause of atelec tasis is complete bronchial obstruction The air contained in the lung distal to the block is absorbed into the blood stream in a matter of hours During this absorption the portion of lung shrinks pro *gressively in volume and the sub atmospheric intra* pleural pressure becomes even lower In the majority of cases probably due to local anoxaemia and the increasing negative pressure there is some exudation of fluid into the alveolar spaces which contributes to the density and homogeneity of the shadow seen on radiographs The site of the obstruction determines the extent of the atelectasis which may involve an entire lung a lobe a segment or multiple lobules Where the initial obstruction has been a large plug of sputum in a major bronchus this may not be demonstrable by the time atelectasis is complete The explanation lies in the fact that the consistency of sputum allows it to be sucked farther and farther down the bronchial tree as the distal

the discouragement of smoking Infection in the upper respiratory tract should be treated but operations to correct simple structural abnormalities seldom help the asthma and are not recommended

Further environmental control in the patient s home is often necessary Domestic pets should generally be discouraged since allergy to them may be acquired but those already in existence should not be ruthlessly destroyed unless clearly incriminated by positive skin test or improvement in the patient s asthma following their temporary removal and aggravation on their return Measures to obtain a bedroom as free from dust as possible are advocated for patients whose attacks occur particularly at night This necessitates removal of all feather pillows mattresses and eiderdowns heavy carpets and curtains linoleum on the floor is permitted Ideally a rubber mattress and pillow and rubber slip mats should be substituted but where this expense is too great cotton mats can be used and laundered frequently and kapok mattress and pillow can be encased in plastic sheeting Only the minimum of clothing furniture and books should be allowed in the room which should be cleaned with a vacuum cleaner daily and only damp dusting is permitted These measures create a bare and unattractive room but in severe cases are well worth while

It may be justified to regard asthma as a psychosomatic disorder and undoubtedly emotional upsets chronic anxiety and over excitement are aggravating factors in many cases The patient is frequently aware of the relationship but such overt psychological disturbances are seldom the whole cause and it is a mistake to regard all asthmatics as neurotic and in need of psychoanalysis Simple explanation by the doctor may help the patient in his adjustment to irremediable and difficult life situations but where there is reason to suspect a deep emotional conflict the help of a psychiatrist should be obtained

Detection of Allergy and Desensitization A painstaking history of the patient and his family is the most reliable method of detecting clues suggesting an allergic basis to asthma Exceptionally a patient presents with a clear cut story identifying a single allergen the asthma only occurring on exposure to it and at no other time In some as the history unfolds of aggravation during visits to the country inhaled pollen may be suspected Food allergies are usually more difficult to detect but are an uncommon cause In many patients however the attacks are completely irregular and no environmental factor can be detected

Skin Sensitivity Tests Some enthusiastic practitioners carry out these tests routinely on all asthmatics and advocate a course of desensitizing injections containing a mixture of all the substances causing a skin reaction Such measures are un rewarding and are not recommended having regard to the fact that injections of saline given with th same enthusiasm can produce equally good but temporary results It is not uncommon for asthmatics to show skin hypersensitivity to a wide variety of injected allergens and equally common for them to react to none Where however a distinct suspicion of allergy has been aroused by the history skin tests may confirm it

Stock testing solutions are made by various firms *e g* Allen and Hanbury, Bencard Limited and instructions accompany each outfit The tests are made on the skin of the forearm either by scratching through a small drop of the solution or by the intradermal injection of 0 05 ml A control test on the other forearm should always be made with the solvent alone The field is narrowed by testing first with the group solutions *i e* mixed inhalants cereals meats fish etc A wheal evident within 15–30 min indicates a positive reaction and the individual members of that group are subsequently tested in the same way An injection of adrenaline should always be at hand when these tests are performed in case asthma is precipitated This precaution is also essential whenever it is necessary to give an injection of foreign serum to an asthmatic and a skin test dose of 0 1 ml should always be given first intradermally

If one or two specific allergens are discovered it may be possible for the patient to avoid them in the future Where it is not possible desensitization may be attempted by subcutaneous injections of gradually increasing amounts of dilute solution of the specific allergens prepared by the makers The procedure is tedious and the duration of desensitization unfortunately variable but some patients receive prolonged and occasionally permanent benefit

Physiotherapy (see p 385) The chronic asthmatic can be helped considerably by the skilled physiotherapist even though tests of pulmonary function may not reveal a substantial objective improvement. The first lessons should be individual instruction in relaxation and until this is mastered no benefit will accrue from breathing exercises

Drugs In chronic cases a state of mild bronchospasm and mucosal congestion persists between the acute episodes and such cases benefit from more continuous therapy Ephedrine hydrochloride is useful for this purpose beginning with 30 mg (0 5 gr) *t d s* the last dose being taken not later than 6 p m in order to avoid insomnia The optimal dose varies widely and should be determined in each patient by gradually increasing the amount until the

slight enough to be ignored but some degree of fever is usual and should suggest the possibility On the other hand when a whole lung or major portion of a lung collapses quickly (massive collapse ') there is a dramatic onset with pain urgent dyspnoea tachycardia cyanosis and fever In extreme cases the clinical picture is that of shock Cough is slight or absent early on but later becomes productive and the expectoration of a considerable quantity of mucopurulent sputum is often the prelude to recovery

Atelectasis of limited extent may be undetectable except by radiography In many cases however abnormal signs are found at one or other lung base The chest wall may be retracted and expansion diminished the apex beat is displaced towards the affected side the percussion note is impaired Breath sounds may be absent diminished or bronchial depending on the degree of patency of the bronchi and will be accompanied by corresponding diminution or increase in vocal fremitus and resonance There are no particular adventitiae over the area of collapse but scattered rhonchi are often audible and râles are common during the stage of resolution

Radiological Examination Characteristic shadows which vary from a broad linear streak to total opacity of one hemithorax are recognizable by the trained eye and are accompanied by the compensatory changes already outlined

Course and Complications If the retained sputum can be dislodged and coughed up the lung re aerates and recovery follows Some degree of infection is present in most cases and unless prompt re-expansion can be achieved pneumonia or suppuration may develop in the collapsed region Bronchiectasis is a common sequel if the atelectasis persists

Differential Diagnosis Primary bacterial pneumonia seldom occurs soon after operation cough and evidence of pleurisy are present at the onset and the mediastinum remains central Pulmonary embolism is distinguished by its later onset—practically never before the fifth post operative day by the occurrence of haemoptysis the absence of cardiac displacement and signs of phlebothrombosis in the legs Pleural effusion gives a greater degree of dullness extending upwards in the axillary line and any displacement of the apex beat is to the opposite side Any doubt is usually resolved by radiography of the chest

Treatment 1 *Preventive* The danger is greatest in patients already suffering from bronchial catarrh and much can be done to prevent the complication by careful planning of the operation and pre operative treatment of the chest condition Only essential surgery should be performed on bronchitic patients during the winter months Where the patient will not suffer by delay the operation should be deferred until the spring or summer when a natural remission in chest symptoms usually occurs Patients should be admitted 10 days prior to the proposed operation and during this time should refrain from smoking and should be given postural drainage for the lower lobes and instruction in breathing exercises Any obvious bronchial infection will require a course of chemotherapy and the patient should be taught the importance of effective coughing in the early post operative period even though this will be painful

Immediately after operation the semi-conscious patient should be gently turned to alternate sides every two hours and be propped up as soon as fully conscious if the type of operation permits Restriction of the lower chest by bandages must be avoided coughing should be encouraged by supporting the patient in the upright position or leaning a little forwards at the same time applying firm pressure with the hand over the abdominal wound Where emergency surgery has been necessary on a patient with much sputum atelectasis should be anticipated and additional precautions are advisable At the end of the operation the bronchial tree may be aspirated through a catheter or bronchoscope and the lungs fully aerated by carbon dioxide inhalation Where possible the prone position with head turned to one side should be adopted Modified postural drainage by raising the foot of the bed with the patient lying for a quarter of an hour on each side alternately should be given three or four times daily An inhalation of 1 per cent isoprenaline may be taken immediately before each period of tipping Alternatively or in addition inhalations of Alevaire (Bayer Products Limited) from a nebulizer for ½ to 1 hr t d s will effectively loosen viscid sputum The isoprenaline and Alevaire can be given together if mixed immediately before use Hand operated atomizers are inadequate for this purpose as a fine mist is essential but there are several efficient nebulizer units on the market operated either from an oxygen cylinder or electrically In between the periods of postural drainage full chest excursion can be encouraged by hourly inhalations of 5 per cent carbon dioxide in oxygen to the point of hyperpnoea The patient should be allowed out of bed and encouraged to walk about as soon as the surgical condition permits

2 *Curative* In the established case treatment consists of an intensification of the measures described for prophylaxis and the administration of a suitable antibiotic usually penicillin 250 000 to 500 000 units 6 hourly The time spent in postural drainage should be increased to several hours daily and percussion and vibration should be given to

air is absorbed At each bronchial bifurcation it may divide and finally it is distributed in the form of several small plugs occluding the bronchioles

Secondary Effects The diminution in volume of the lung which accompanies atelectasis is compensated for in various ways Unobstructed lung distends (compensatory emphysema) and the mediastinum moves towards the affected side The hemidiaphragm is displaced upwards and if there is extensive atelectasis the thoracic wall may sink inwards When the atelectasis involves no more than a segment the surrounding compensatory emphysema is usually sufficient to restore the balance of intrathoracic forces and displacement of viscera is seldom seen

Persistent atelectasis is a common precursor of bronchiectasis and the relationship is discussed on p 331 Briefly where major bronchial obstruction persists and consequently atelectasis the accumulation of infected secretion beyond the block causes the bronchi to distend Where atelectasis is associated with sputum blocking a large number of terminal bronchioles the bronchi tend to dilate in response to the pressure difference within and without their walls Lung which is atelectatic is prone to infection and bacteria may be introduced by the obstructing object itself An inflammatory exudate then forms in the collapsed alveoli so that there is a mixture of collapse and consolidation Depending on the virulence and type of the organisms a range of conditions from simple infected atelectasis (aspiration pneumonia) to putrid anaerobic lung abscess may follow Unless infection is introduced at the time of the bronchial obstruction however subsequent infection of an atelectatic segment is less common in the upper lobes than the lower possibly due to the better drainage afforded by gravity

Pathology The affected portion of lung is firm darker in colour than healthy lung smaller than normal and sinks in water Histologically the alveoli are collapsed and airless and often contain inflammatory exudate In long standing cases the whole area may become densely fibrotic

Aetiology and Predisposing Factors The lumen of a bronchus may be obstructed by a foreign body tenacious sputum or a new growth Bronchial strictures are not uncommon following tuberculous bronchitis External pressure by enlarged lymph nodes mediastinal tumours and aortic aneurysms may also occlude the airway Progressive narrowing of the lumen in all these conditions may become complete obstruction with the additional elements of retained secretion and impaired bronchial drainage In childhood and adolescence tuberculous hilar adenitis is a common cause Erosion of a bronchus by a caseous lymph node may cause temporary obstruction which resolves as the lymph node subsides but the process of healing may be accompanied by stricture formation which produces permanent atelectasis The right middle lobe is a common site for this In adults bronchial carcinoma accounts for a high proportion of cases

The removal of secretions from the bronchial tree depends upon cilial action and an effective cough The cilia may be clogged by excessive viscid sputum in such conditions as chronic bronchitis and asthma or be destroyed locally as a result of tuberculous bronchitis bronchiectasis or neoplastic infiltration. In such cases atelectasis from sputum block is always a risk An ineffectual cough particularly when combined with an excessive amount of sputum is a potent cause of pulmonary atelectasis and is the main factor in post operative cases The many other causes include interference with glottic function vocal cord paresis tracheotomy paralysis of respiratory muscles crush injuries of the chest enforced recumbency emphysema comatose states, cachexia and the general enfeeblement of old age

It will be realized that atelectasis occurs in a wide variety of pulmonary conditions and that the clinical picture will depend largely upon the primary disease Additional symptoms and signs other than radiographic evidence attributable to the atelectasis itself may appear only if the atelectasis is extensive rapid in onset or followed by secondary infection

Post-operative Atelectasis

Aetiology The main cause of post-operative pulmonary atelectasis is the retention of secretion in the bronchial tree due to a combination of several factors During and following surgery the cough reflex is suppressed for many hours by general anaesthesia sedative and pain relieving drugs and by the voluntary efforts of the patient to avoid pain The anaesthetic is probably the least important since the complication occurs after local regional or spinal anaesthesia Upper abdominal operations are especially prone to be followed by basal pulmonary collapse and it can be shown that diaphragm excursion is reduced for several days following operation Where in addition such surgery has to be performed on patients with one or more of the general predisposing factors mentioned in the preceding paragraph the hazard of post operative atelectasis is proportionately greater

Clinical Picture Symptoms usually start abruptly on the second third or fourth post operative day with local or central chest pain and breathlessness If the area involved is small symptoms may be

further symptoms due to complications appear varies from a few hours to months or even occasion ally years Objects of vegetable origin soon produce symptoms and signs of an acute purulent bronchitis with atelectasis and infection distal to the obstruc tion Mineral objects may produce segmental or lobar atelectasis which may remain silent for months but eventually infection in the collapsed area supervenes with increasing cough and sputum which becomes purulent and often blood stained The virulence of the secondary infection and failure to remove the foreign body are the two factors which determine whether the patient will present with an acute pneumonia or symptoms of chronic pulmonary suppuration due to secondary bronchi ectasis or lung abscess

Diagnosis. A clear cut history of something go ing down the wrong way should never be ignored The occurrence of atelectasis pneumonia or broncho pulmonary suppuration following surgery on the upper respiratory tract should arouse sus picion Provided the possibility is considered a detailed interrogation will often reveal a choking episode which has been forgotten by the patient Radiography will show a foreign body opaque to X rays but several views and exposures may be re quired before its presence and position can be iden tified In all cases of doubt bronchoscopy is essential

Treatment. Immediate removal of the foreign body by a skilled bronchoscopist is required and the great majority can be successfully removed in this way Very rarely thoracotomy is necessary Natural expulsion should not be awaited as it seldom hap pens Not infrequently the object migrates particu larly from the left side to the right so that radiographs should be repeated immediately before the bronchoscopy The operation is followed by postural drainage and a course of chemotherapy penicillin being the first choice but determined sub sequently by the bacterial flora of the sputum In most cases the pulmonary infection will clear com pletely but if permanent structural changes have occurred with persistent suppuration surgical re section of the diseased area may be necessary

BRONCHIECTASIS

Definition Dilatation of the bronchi is usually associated with inflammatory changes in the walls

Aetiology A rare congenital variety usually cystic sometimes occurs in identical twins or with other congenital abnormalities as in the combination of bronchiectasis sinusitis and dextrocardia which constitutes Kartagener s syndrome Most cases are acquired although the mechanism by which the dilatation is produced is not always clear Often it is due to bronchial obstruction combined with in fection Persistent obstruction to a bronchus results first in atelectasis Infection distal to the obstruction causes increased secretion which distends the bron chi particularly as their walls become weakened by the inflammatory process Any bronchial obstruc tion may therefore be complicated by bronchiectasis but common causes are foreign bodies bronchial carcinoma and enlarged hilar nodes The longer such obstruction persists the greater is the damage to the walls of the bronchi by the infection and the more likely is the bronchiectasis to remain per manent even though the obstruction may subse quently be removed Relief of the obstruction and consequent establishment of bronchial drainage while infection is still confined to the mucous mem brane is frequently followed by return of the bronchi to normal calibre (temporary or reversible bron chiectasis) When sputum is the obstructing agent the mechanism is somewhat different Pulmonary atelec tasis again follows the complete bronchial occlusion and the normal atmospheric pressure from above combined with the increasingly subatmospheric pressure distally causes the aspiration of the sputum down into the terminal bronchioles The portion of lung remains atelectatic as the bronchioles are plugged with sputum but the bronchi proximal to these plugs are patent Being elastic structures they dilate as a result of the positive pressure inside the lumen and the negative pressure beyond their walls Once again the condition may revert to normal if the sputum plugs can be dislodged within a few weeks but the longer they remain and the more severe the superadded infection of the bronchial walls the greater the chances of permanent bronchi ectasis It is this type of bronchiectasis which may complicate any broncho pulmonary infection in which viscid or copious sputum is not freely expec torated The small bronchi of infants are easily obstructed and severe whooping cough or measles are potent causes Fortunately the prompt and efficient treatment of pneumonias to day has resulted in a progressive decline in the incidence of this disease

Pathology The lower lobes are the most frequent site of the disease According to the general shape of the dilated bronchi the following types are recog nized *tubular* (or cylindrical) when the dilatation is more or less uniform *fusiform* when they are spindle shaped and *saccular* (or cystic) when the distal bronchi are distended to form more or less spherical cavities The bronchial epithelium exhibits varying degrees of acute and chronic inflammation and ulceration local hyperplasia or squamous

the chest in addition In most cases the lung re expands within 48 hr *If it does not do so broncho scopic aspiration should be considered* as its chances of success diminish with further delay owing to the aspiration of sputum into the smaller bronchi out of reach of the bronchoscope

FOREIGN BODIES IN THE RESPIRATORY PASSAGES

Any of the conducting air passages may be partially or completely obstructed by foreign bodies They should be removed as soon as possible because of the risk of complications Young children are more frequent victims than adults because of their habit of putting all manner of objects into their mouths In adults however, the female practice of holding pins and the craftsman s habit of holding *screws and tacks in the mouth provide examples*

Nose

Foreign bodies in the nose *seldom occur in adults* but when they do the history is usually quite clear In infants however who cannot give a clear account of their deeds or symptoms such articles as beads buttons and small playthings occasionally find their way into the nasal passages The condition should be suspected when a child presents with unilateral *nasal discharge with or without frequent sneezing* and the object should be removed with suitable instruments under local or general anaesthesia

Pharynx

Foreign bodies in the pharynx are often small and pointed such as a fish bone or pin the point being driven into the tonsil or back of the tongue during swallowing Small pieces of bone and occasionally pills sometimes lodge in the pyriform fossa or vallecula They cause pain *on swallowing* and frequent hawking and coughing The treatment is removal by indirect or direct laryngoscopy

The glottis may be partly or completely obstructed by a large bolus of food or a denture A violent slap on the back while eating is a common cause of such accidents If the obstruction is complete death from asphyxia will follow in a few minutes if it is not removed The emergency treatment consists in immediate removal by the forefinger through the mouth but *if the attempt is unsuccessful a tracheo* tomy should be performed and the foreign body subsequently removed by direct laryngoscopy

Larynx

A foreign body in the larynx gives rise to constant coughing hoarseness stridor and sometimes dysphagia Even a small foreign body may soon cause complete obstruction because of laryngeal spasm and oedema No time should be lost in its removal which is most easily carried out by direct laryngoscopy

Trachea

A tracheal foreign body is an uncommon event Violent cough and dyspnoea are usual often in spasms The patient may feel and the physician may hear with a *stethoscope the article rattling up* and down the trachea Subsequent ulceration and oedema of the mucous membrane causes increasing dyspnoea and complete occlusion may ensue if the object is not removed by bronchoscopy

Bronchi

Foreign bodies in the bronchi are virtually always inhaled although occasionally they arise from gun shot and shrapnel wounds of the chest Factors which predispose to their inhalation are laughing gasping or sobbing while eating or holding things in the mouth states of unconsciousness operations on the upper respiratory tract including dental extractions and pharyngeal paralysis The foreign body descends the bronchial tree a variable distance lodging most commonly in the lower lobe bronchi *The more vertical course of the right main* bronchus accounts for the majority being found on the right side The nature of the foreign body has some bearing on the subsequent local reaction in the bronchus Metal and stone objects incite little inflammation pieces of bone or tooth a moderate local reaction whereas vegetable matter such as nuts beans and seeds cause a rapid and intense reaction

Immediate Effects. There is usually a choking or coughing fit as the object is inhal d through the *larynx but no such story* will be obtained if the accident has occurred during unconsciousness. *Once* the foreign body is arrested in one position the cough may cease for the time being At this stage there may be no physical signs in the *lungs but* occasionally a localized wheeze is detected and very rarely signs of obstructive emphysema on one side *This is essentially an over-distension of one* lung or lobe produced by the check val e action of a foreign body of such size and shape as to occlude the bronchus completely in expiration *but to allow* air to enter during inspiration or during coughing The chest on that side appears bulged the percussion note is hyperresonant or tympanitic the breath sounds are absent and the mediastinum displaced to the opposite side These signs closely resemble those of pneumothorax and radiological examination may be necessary to distinguish them

Subsequent Effects The silent period before

conditions in which chronic cough and purulent sputum are features Chronic bronchitis pulmonary tuberculosis lung abscess bronchial carcinoma and an empyema may produce the same symptoms Methodical investigation by radiographs sputum tests bronchoscopy and bronchography usually establish the condition with certainty and demonstrate whether the bronchiectasis is the main condition or merely occurring in association with some other disease

Complications and Prognosis. That some cases are reversible with prompt treatment of the underlying cause has been noted In established cases the symptoms can be controlled in the majority by conscientious treatment and the condition has then little tendency to progress In generalized infected bronchiectasis and in patients who neglect treatment, only a partial control of symptoms is possible and the prognosis as regards complications and premature death is correspondingly worse An empyema may form at any stage and death may occur during one of the recurring acute infective exacerbations or ultimately from cardiac or respiratory failure Rarely an uncontrollable haemoptysis terminates the illness An unforeseen complication is cerebral abscess and after many years of pulmonary suppuration amyloid disease occasionally develops

Treatment. (*a*) *Preventive* The key to prevention is the thorough treatment with antibiotics and physiotherapy of all acute pulmonary infections particularly during childhood Medical care should continue until complete clinical and radiological resolution are assured The same principles apply to adults and where surgical operations are planned the prophylactic measures outlined for the prevention of post operative atelectasis should be instituted

(*b*) *Symptomatic and Curative* Surgical resection of the diseased area provides a permanent cure in some cases Selection of such cases however requires great care and a wide experience of the disease Patients with localized bronchiectasis producing symptoms which cannot be relieved medically are the most suitable but should not be submitted to surgery without thorough trial of antibiotics and postural drainage Recurrent severe haemoptysis is another indication for surgery Bilateral segmental resections are now possible but due regard must be had to the risk of pulmonary insufficiency where extensive resections are contemplated Operation is seldom justified over the age of forty and is best carried out in late childhood or adolescence

Conservative treatment aims at keeping the affected bronchi as empty and dry as possible and combating infection with suitable antibiotics Guidance in the choice of occupation and place of residence and general advice on maintenance of fitness are important and follow the lines indicated for chronic bronchitis The upper respiratory tract including the teeth should receive attention and be kept as healthy as possible Postural drainage is the mainstay of medical treatment and is discussed in greater detail under Physiotherapy in Diseases of the Chest, p 384 Its object is to employ the force of gravity to drain the sputum in the dilated bronchi towards the main bronchi and trachea where it will incite the cough reflex and be expectorated In brief bronchi which take a forward course are drained with the patient supine those running backwards with the patient prone bronchi running in an upward direction from the carina drain with the patient propped up and those running downwards with the patient in the head-down position In addition inclination to one or other side is necessary in unilateral cases Reference to the diagrams Fig 16 1 p 301 and the illustrations Plates 16 12 and 16 13 will demonstrate the application of these principles In severe cases several hours postural drainage each day will be required until maximum benefit is obtained and during the periods of dependent drainage pummelling the chest, vibrations and instruction in forced expiration and coughing should be given by a trained physiotherapist to assist in dislodging the secretions Potassium iodide 1 g (15 gr) t d s orally or detergent aerosol inhalations can also be given if the sputum is particularly tenacious A course of antibiotics is given at the same time depending on the flora of the sputum either a combination of penicillin 500 000 units 6-hourly and streptomycin 1 g daily or tetracycline 500 mg 6-hourly is recommended and should continue for a fortnight or longer in the absence of toxic effects and resistant organisms After this *initial intensive course of treatment, and when* maximum improvement has occurred it can usually be maintained by regular postural drainage for 15–30 minutes morning and evening Severe cases may require a period of drainage in the middle of the day also but a regular routine is important and the patient should organize his life to devote the necessary time to it During the summer it is sometimes possible to reduce the time spent in drainage and during the winter or when the patient has a cold the time should be correspondingly increased Even correct management will not altogether prevent exacerbations of infection from time to time but it will considerably reduce their frequency Any such exacerbation should be treated early with a further course of chemotherapy and longer periods of

metaplasia are commonly seen The elastic and muscular coats are partly destroyed and replaced by fibrous tissue The surrounding lung may be atelectatic and, microscopically areas of pneumonia emphysema or fibrosis are seen Evidence of recent or past pleurisy will also usually be found over the affected area Enlarged anastomotic channels between bronchial and pulmonary vessels can sometimes be demonstrated and may account for the common symptom of haemoptysis Among the organisms which may be cultured from the pus within the dilated bronchi are pneumococci streptococci staphylococci *H influenzae* and various anaerobes

Clinical Picture Occasionally cases are seen especially affecting the upper lobes in which no symptoms are admitted but most cases present with one or more of the following features productive cough haemoptysis and recurrent chest infections

Productive Cough The history of chronic cough frequently goes back into childhood and may date from an acute respiratory infection such as whooping cough measles or pneumonia The amount and character of the sputum vary with the extent of the disease and the type of infection Most commonly it is mucopurulent or purulent an average case producing an ounce or two each day and a severe case as much as a pint The thick yellow sputum has a somewhat characteristic sickly smell In other cases where there is much stagnation it is greenish with a most objectional putrid odour and the patient s friends may shun him because of the unpleasant halitosis The suggestive evidence provided by inspection of the sputum may be lacking in children who usually swallow it but by tipping them into a suitable position for postural drainage and encouraging them to cough and spit a suitable specimen can usually be obtained at the time of the examination Changes in position often precipitate cough and expectoration and patients frequently relate how bouts of coughing are initiated by lying down at night or getting up in the morning

Haemoptysis Bronchiectasis is one of the commoner causes of blood spitting in young adults and second only to pulmonary tuberculosis It may be the presenting symptom and tends to recur periodically Where the disease affects bronchi which drain relatively freely recurrent haemoptysis may be the only symptom (' dry or haemorrhagic bronchiectasis ') Blood staining and flecking of the sputum is very common in established cases when the blood is probably derived from granulation tissue in the abnormal bronchi but cases with frank haemorrhage probably bleed from anastomotic channels between bronchial and pulmonary vessels

Recurrent Chest Infections Patients with bronchiectasis are liable to recurrent exacerbations of infection in the diseased area often precipitated by coryza or a similar upper respiratory infection Chronically infected sinuses may co exist with bronchiectasis and provide a source for periodic re infection of the bronchial tree The history often reveals repeated attacks of pneumonia or pleurisy on the same side each time and such attacks may date from some chest illness following a surgical operation

Dyspnoea is seldom the symptom for which advice is sought but in many cases is admitted at interrogation Deterioration in general health accompanies extensive or long standing infected bronchiectasis The patient is always a little below par underweight, with poor appetite lack of energy slight cyanosis some anaemia and general debility Clubbing of the fingers and toes is a common clinical sign in such cases Symptoms and signs of a metastatic cerebral abscess are occasionally the reason for seeking medical treatment but such cases are rare to day and the chest symptoms are always present in addition

The signs in the chest vary considerably depending on the extent of the disease and the amount of sputum in the bronchi at the time of examination They may also vary in the same patient from day to day A localized area of so called dry bronchiectasis may give no abnormal signs and the patient s nutrition and general health do not suffer All the signs of lower lobe atelectasis more commonly on the left side may be apparent but the commonest abnormality is an area of persistent coarse or medium rales In generalized cases moist sounds are heard throughout the lungs clubbing is present chest deformity is common and the general condition is poor

Radiological Examination Plain radiographs may be normal but exaggerated lower lobe striations or areas of coarse mottling are common Typical shadows of segmental or lobar atelectasis may be seen a penetrating film being necessary to demonstrate them behind the heart shadow In the saccular type there may be multiple cystic areas with or without fluid levels

Diagnosis The history clinical evidence and X ray appearances are often sufficient for diagnosis but bronchography is essential to determine the exact location and extent and is necessary to exclude the disease in cases of doubt If there is much sputum this examination should be preceded by a period of postural drainage in order to empty the bronchi and allow the iodized oil to enter them Typical bronchographic appearances are shown in Plate 16 2

Differential Diagnosis This includes a variety of

Clinical Picture In some cases an upper respiratory infection precedes the illness or there may be a history of exposure or chill The onset is abrupt with shivering malaise pleural pain fever and a dry painful cough In infants a convulsion replaces the rigor vomiting is frequent and meningism is sometimes observed particularly in upper lobe pneumonia The temperature rises rapidly to 103 or 104 F and may be accompanied by severe headache and delirium The skin is hot and dry the face flushed and cyanosis may be evident A labial herpes commonly appears in the first few days The initial cough produces only a little mucus but in the next day or two the sputum becomes mucopurulent and is often stained pink or brownish (rusty sputum) Breathing is rapid and shallow and the accessory muscles of respiration may be seen in action In lower lobe pneumonia the pain from the diaphragmatic pleurisy is commonly referred to the tip of the shoulder or to the abdomen

The natural course of the disease is practically never observed to day since it is modified by effective treatment Untreated however symptoms continue with high fever increasing exhaustion and sometimes peripheral vascular failure In favourable cases a crisis occurs 5–11 days after the onset dramatic improvement taking place within the space of a few hours The temperature falls to normal toxaemia abates sweating occurs and the exhausted patient falls to sleep to awake mentally clear and much refreshed In other cases the fever abates gradually over the course of several days (lysis)

Examination of the Chest During the early stages the commonest abnormality is an area of fine râles heard in inspiration Movement may be diminished the percussion note impaired the breath sounds diminished and a pleural rub may be detected Signs of consolidation (*see* p 312) often appear within 2 or 3 days of the onset During resolution râles increase both in number and coarseness chest expansion slowly improves and the percussion note and breath sounds gradually revert to normal Abnormal signs may be detected for a week or two after the temperature has subsided but in the absence of complications eventually clear completely

Radiological examination of the chest shows a more or less uniform opacity of the affected segment or lobe Plate 16 3 or similar scattered opacities due to lobular consolidation usually in both lower lobes

Prognosis In otherwise healthy adults provided specific treatment is given early in the disease complete recovery is the rule The overall mortality of 5 per cent occurs particularly among the elderly the previously debilitated patients with cardiac insufficiency and those in whom treatment has been delayed

Complications Occasionally the infection may spread to involve other lobes Abscess formation is an exceptionally rare complication of pneumococcal pneumonia as is also fibrosis of the lung Dry pleurisy is almost always present and a sterile serous effusion is not uncommon Empyema is an important complication but its incidence has fallen greatly since the introduction of chemotherapy It should be suspected when the response to specific treatment is poor or when the fever returns after having settled and it will be discussed further in a later chapter

Blood stream spread of the infection to other organs is occasionally responsible for pericarditis endocarditis arthritis meningitis or peritonitis Toxic hepatitis and glomerulo tubular nephritis have also been reported Congestive heart failure with or without auricular fibrillation may be precipitated in patients with poor cardiac reserve and severe cases may develop peripheral vascular failure Delayed resolution is very uncommon provided the affected lung was previously normal and this diagnosis should never be accepted until local complications and underlying broncho pulmonary disease have been excluded

Differential Diagnosis In most cases diagnosis can be made from the clinical features supported when necessary by a white-cell count sputum tests and radiograph of the chest Other forms of pneumonia considered later can sometimes be distinguished clinically but often require laboratory investigation for exact diagnosis *Pulmonary infarction* may give rise to difficulty and a careful search must be made for an embolic source especially in the heart and legs fever is seldom as high as in pneumonia and frank haemoptysis is more common *Pulmonary atelectasis* may give similar signs but mediastinal displacement to the affected side is detectable clinically or radiologically *Acute dry pleurisy* may have a similar onset but no signs of consolidation develop *Tuberculous pleural effusion* usually starts more insidiously cough and sputum are much less the physical signs are those of fluid and in cases of doubt the chest should be needled under local anaesthesia Reference of diaphragmatic pleural pain to the abdomen may simulate an acute abdominal emergency In doubtful cases a chest radiograph is the best safeguard Conversely acute inflammatory conditions in the subdiaphragmatic region may simulate pneumonia at the onset and may be distinguished only by the subsequent clinical course

Treatment *See* under 'Treatment of Pneumonia p 338

drainage The organisms in the sputum change from time to time and periodic checks should be made in the laboratory Neglected or inadequately treated patients are apt to become infected with resistant coliforms Neomycin by inhalation is sometimes effective in such cases

PNEUMONIA

Definition Inflammation of lung tissue with alveolar exudation resulting in pulmonary consolidation

Types Now that effective treatment is available for most cases of pneumonia the older classification into lobar and broncho pneumonia based simply on morbid anatomical distribution of lesions has given place to one based on aetiology For completeness such a classification must include chemical irritation allergic exudation and parasitic invasion of the lung but for practical purposes pneumonia is due to infection by one or more of a large number of bacteria including viruses Some of these organisms are sufficiently pathogenic to invade normal lung—*the specific infective pneumonias* others succeed in doing so only when the defences of the respiratory tract are impaired locally or generally for various reasons to be discussed—*non specific infective pneumonias* For general purposes therefore pneumonia may be classified as follows—

A *Specific Infective Pneumonias*

1 *Bacterial*
   Strep pneumoniae (pneumococcal pneumonia)
   K pneumoniae (Friedländer s bacillus)
   Strep haemolyticus
   Staph pyogenes
   H influenzae
   M tuberculosis

   Rare organisms include—
   S typhi
   P pestis (pneumonic plague)
   P tularensis (tularaemia)
   B anthracis (woolsorter s disease)

2 *Viral*
   Psittacosis ornithosis group
   Others ("primary atypical pneumonia")

3 *Rickettsial* e g Q fever

4 *Parasitic* Fungi helminths flukes and plasmodia etc

B *Non Specific Infective Pneumonias* (*Aspiration Pneumonia*)

1 Localized (infected atelectasis)

2 Diffuse (broncho pneumonia hypostatic pneumonia terminal pneumonia, etc)

C *Miscellaneous Pneumonias*

1 Allergic (Loeffler s syndrome pulmonary eosinophilias)

2 Physico chemical (radiation pneumonitis irritant gases lipoid pneumonia)

Such a classification is necessarily imperfect as mixed infections are frequent Thus the pneumonia which complicates influenza or the acute specific fevers of childhood is due to combined viral and bacterial infection the one predisposing to the other Similarly pneumonia initiated by irritant gases is complicated by secondary bacterial infection Both in the specific and non specific groups suppuration may occur with the formation of lung abscess The classification could therefore be extended by adding suppurative and non suppurative groups However this renders the classification unwieldy and pulmonary suppuration will receive separate consideration

A Specific Infective Pneumonias

1 Bacterial

Pneumococcal Pneumonia

Aetiology and Predisposing Factors The infecting organism is *Strep pneumoniae* (pneumococcus) a Gram positive diplococcus of which there are many types Types I II and III are responsible for most cases of acute specific pneumonia the higher types being less pathogenic and often found as commensals in the upper respiratory tract Cold damp weather predisposes to the infection 70 per cent of cases occurring during the winter and spring months An upper respiratory infection frequently precedes the illness which is also common in those debilitated by general ill health from other causes malnutrition exposure chronic alcoholism and extremes of age Case to case spread is uncommon but small epidemics are reported

Pathology Infection is acquired by inhalation the organism passing through the bronchial walls to invade the interstitial tissues of the lung and bacteraemia is often present in the early stages Alveolar exudation follows with consolidation of lung tissue which is often segmental or lobar in extent but may be of patchy lobular distribution (broncho pneumonia) An over lying pleurisy accompanies these changes When fully formed the exudate contains fibrin red cells many polymorphs and some mononuclears Enzymes from the degenerate leucocytes initiate the stage of resolution by liquefaction of the exudate which is then removed by phagocytosis and expectoration Permanent structural damage to the lung is uncommon resolution usually being complete A polymorphonuclear leucocytosis of the order of 15 000–25 000 W B C per mm^3 is usually present and during the febrile stage albuminuria is common

tests Anti bacterial treatment takes pride of place but the general measures remain important and their neglect especially at the extremes of age may determine a fatal outcome in spite of chemotherapy

General Management Admission to hospital will be decided by consideration of the severity of the illness the home conditions unusual features casting doubt on the diagnosis and the presence or suspicion of complications Where the gravity of the illness demands transfer to hospital 1 mega unit of crystalline penicillin G should be given beforehand The average case however can be treated at home provided adequate room and nursing care are available Young infants and frail or elderly adults should avoid contact in the early stages as some cases are infectious

The patient should be kept warm in bed in a well ventilated but draught free room maintained at a temperature of around 65 F The orthopnoeic position is advisable in most cases and clothing should be light non constricting and easily removable Sputum should be disinfected and records kept of the temperature pulse respiration and fluid balance Mouth hygiene attention to pressure areas and general bed comfort are important points in nursing care Diet is relatively unimportant and can be dictated by appetite and taste but a minimum of 4 pints of fluid in the 24 hr should be taken Flavoured milk drinks egg flips broths and sweetened non effervescent fruit drinks supply the necessary volume and also provide light nourishment which can be augmented with thin bread and butter biscuits sponge cake junkets jellies custard ice-cream etc according to taste As the temperature subsides and the appetite improves small meals of eggs cereals fish chicken creamed potatoes and vegetable purées become acceptable

Non specific Treatment Non specific or symptomatic treatment may be required for the following symptoms in particular—

Cough The frequent unproductive initial cough aggravates pleural pain prevents sleep and exhausts the patient It may be relieved by Linct Methadon 4–8 ml (1–2 dr) or codeine phosphate 30–60 mg in a pill or linctus Morphia is permissible for the first few nights if the patient is not cyanosed As the cough becomes productive expectoration should be encouraged by supporting the patient sitting forward during coughing and by frequent hot drinks expectorants and steam inhalations Inhalations of a detergent aerosol *e g* *Alevaire* from a suitable atomizer connected to an oxygen cylinder are often helpful and as soon as practicable short periods of physiotherapy and postural drainage should begin

Pain Pleural pain is slight in some cases and agonizing in others Local heat and an oral analgesic *e g* Tab Codeine Co will relieve the less severe cases A hot water bottle is preferable to the time honoured kaolin poultice since it is always available needs no constricting bandage around the chest to keep it in place is easily renewed and is not messy Severe pain may require morphine 10–15 mg (⅙–¼ gr) but in emphysematous or cyanosed patients pethidine 50–100 mg is preferable An alternative measure is to infiltrate the parietal pleura locally with procaine

Restlessness and Delirium These are common in the early stages and sedative drugs should not be administered until such causal and aggravating factors as high fever anoxia dehydration and toxaemia have been remedied as far as possible Tepid sponging oxygen and increased fluid intake if necessary by the intravenous route will relieve most of these but the toxaemia will only lessen with the response to chemotherapy If a sedative is required chloral hydrate 1–2 g (15–30 gr) is safer than a barbiturate Paraldehyde 4–8 ml (1–2 dr) is also effective and if necessary 5–10 ml can be given intramuscularly

Insomnia The relief of pain distressing cough and high fever may permit natural sleep but if an hypnotic is required in addition chloral hydrate is safe and effective

Cyanosis Oxygen should be given to all cyanosed patients as anoxia is an important causal factor in delirium pulmonary oedema congestive failure or circulatory collapse An oxygen tent is useful for young children but for adults a plastic polymask or B L B mask is efficient with an oxygen flow of 3–6 l/min Appropriate measures for congestive failure may be required

Peripheral Circulatory Failure In severe cases a state of shock may develop quickly It is heralded by pallor cold blue extremities sweating rising pulse rate and falling blood pressure The most effective treatment for this is probably hydrocortisone 25–50 mg intravenously 4 hourly together with an intravenous drip of 5 per cent glucose containing noradrenaline 4–8 mg per litre

Abdominal Symptoms Constipation is common in the first few days but watch should be kept for abdominal distension (tympanites) which adds further to respiratory embarrassment It should be treated early by the passage of a flatus tube or the administration of a turpentine enema Prostigmine 1 mg subcutaneously should be tried if other measures fail

Specific Treatment *Choice of Anti bacterial Drug* Treatment should begin with anti bacterial drugs known to be effective in the majority of cases A wide choice of remedies confronts the physician

The other bacterial pneumonias have many features in common with pneumococcal pneumonia but some of them can be suspected on clinical grounds Generally speaking however the specific organism can be identified only when it is grown from the blood or in predominant growth from successive samples of sputum

Friedländer's Pneumonia

A rare but severe disease due to infection with *Klebsiella pneumoniae* (pneumobacillus of Fried lander) The onset resembles the more severe form of pneumococcal pneumonia usually affecting an upper lobe A characteristic feature is the rapid breakdown of the consolidated lung to form abscess cavities from which a brick red or brown sputum is expectorated Mortality is high 60–80 per cent in unrecognized cases and resolution is slow A small proportion who survive the acute stage progress to a chronic suppurative pneumonia with excavation resembling the clinical picture of chronic cavitated pulmonary tuberculosis Streptomycin in large doses is the most effective treatment

Haemolytic Streptococcal Pneumonia

As primary invaders of the lung β haemolytic streptococci are not common but viral infections of the respiratory tract such as measles or in fluenza seem to predispose to infection by them Pathologically they cause a confluent broncho pneumonia, often bilateral with severe inflamma tory changes in the bronchioles and interstitial tissue Organization begins early so that resolution is not infrequently incomplete This infection should be suspected when pneumonia follows a strepto coccal throat infection or influenza and the organ ism is usually plentiful in the sputum Although the onset is usually more gradual the illness is more serious than pneumococcal pneumonia and the complications of pleural effusion and empyema are more frequent

Staphylococcal Pneumonia

Like the haemolytic streptococcus *Staph aureus* may produce a fulminating form of pneumonia complicating influenza The lungs may also be in volved via the blood stream as part of a staphy lococcal pyaemia and occasionally the organism may directly invade the lung particularly in infants The disease is usually severe with high swinging temperature profuse sweats cyanosis and an in creasing cough with purulent sputum which contains large numbers of staphylococci This type of pneu monia has a strong tendency to suppurate forming multiple thin walled abscesses often within a week of the onset and rupture into the pleura with conse quent pyopneumothorax may occur The abscess cavities may persist for months or years after eradi cation of the infection as thin walled cysts resem bling a collection of soap bubbles Treatment is with large doses of penicillin 4 hourly in the first instance Sensitivity tests should always be made as penicillin resistant staphylococci are not un common

Tuberculous Pneumonia

The more acute forms of pulmonary tuberculosis can resemble pneumococcal pneumonia both clini cally and radiologically Often however there is a history of preceding slight cough and sputum lassi tude and loss of weight Haemoptysis is common the sputum is mucopurulent and seldom rusty Ex amination of the sputum for acid fast bacilli is essential in any case of pneumonia not responding to routine chemotherapy

For the rarer forms of bacterial pneumonia and for the parasitic types which are also very un common the student must refer to specialized text books

2 Viral Pneumonia

Virus pneumonia has become a frequent clinical diagnosis in recent years, but it is probable that many cases so labelled are in reality simple aspira tion pneumonias or pneumonias due to organisms insensitive to penicillin The influenza viruses do not cause pneumonia in man although they may in laboratory animals The pneumonia associated with influenza as with measles is caused by a combina tion of the virus and secondary bacterial infection Occasionally it may be of the fulminating variety causing death within 48 hr and in such cases the secondary organism is usually a haemolytic *Staph aureus* A commoner type of influenzal pneu monia develops a few days after the onset of the flu and is due to a variety of pathogenic bacteria including pneumococci streptococci and *H in fluenzae* the lesion in the lung being usually patchy lobular consolidations especially in but not confined to the lower lobes

Viruses known to cause pneumonia are those of the psittacosis-ornithosis group They are trans mitted by birds of the parrot family also by pigeons finches and chickens the virus being ex creted in their droppings and nasal discharges The illness is infectious and may be severe Clinically the onset is characterized by constitutional rather than respiratory symptoms Severe headache rigors vomiting limb pains epistaxis restlessness and delirium are prominent at first Cough with mucoid sputum and moderate dyspnoea are less in evidence



HEALED PULMONARY TUBERCULOSIS

Extensive calcified disease scattered through the right lung Nine rib thoraco plasty on the left side

and different schemes of treatment are equally effective when judged from an overall series Expense and convenience are of some importance in the choice of drugs but there are certain principles more important when dealing with a seriously ill patient in whom rapid control of the infection is essential In such cases the parenteral route of administration is advisable and a bactericidal agent such as penicillin has possible advantages over the bacteriostatic drugs of the broad spectrum type Combinations of antibiotics may delay drug resistance and broaden the anti bacterial spectrum but bactericidal and bacteriostatic drugs should not be given together Penicillin sulphonamides and streptomycin can be given in combination with possible added benefit but they should not be given concurrently with tetracyclines or chloramphenicol Extensive clinical experience and controlled trials have shown that penicillin is unsurpassed in its effect against the commoner organisms causing pneumonia Sulphonamides are effective for routine use in the average case Sulphadimidine or sulphatriad are the safest but should be avoided for patients in whom it is difficult or undesirable to maintain a high fluid intake These include the very old and the very young patients severely dehydrated when first seen and those suffering from nephritis or congestive failure Previous sensitization to sulphonamides is also a contra indication In such patients penicillin is the drug of choice and the first dose should be by injection Except in the gravely ill the long acting preparations or combinations of these with the soluble form can be used but they cause more local discomfort and the sensitization rate seems to be higher Acid stable phenoxymethyl penicillin (Penicillin V) is sufficiently reliable by mouth for continuation of treatment and occupies a particular place in the treatment of children

Suggested Schemes for the Initial Treatment of Pneumonia

Mild case treated at home
Sulphadimidine 2–3 g stat then 1 g 4 hourly *or* Procaine Penicillin G 600 000 units daily + Penicillin V orally 125–250 mg 4 hourly

Case of moderate severity
Fortified Procaine Penicillin (e g Distaquaine Forti fied Seclopen') 400 000 units i m b d together with sulphadimidine as above

Severe case (preferably in hospital)
Crystalline Penicillin G 500 000 units i m 6 hourly together with a course of sulphadimidine

Fulminating case
Crystalline Penicillin G 1 000 000 units i v 2 hourly *or* erythromycin lactobionate 300–600 mg 4 hourly by slow i v injection or infusion

A striking improvement may confidently be expected in most cases within 36–48 hr the temperature falling to normal or near normal and toxaemia abating On occasions only a partial response is evident although the laboratory tests indicate the infection is susceptible to the prescribed treatment. Such a result should dictate trial of a temporary increase in dosage for 24–48 hr rather than a change of antibiotic When the temperature has been normal for two days the dose can be halved and subsequently reduced gradually so that the course of treatment lasts about a week

Failure of Routine Treatment If the expected improvement is not apparent after 48 hr careful re assessment is necessary with regard to (*a*) the infective agent (*b*) complications of the pneumonic process and (*c*) the presence of underlying broncho pulmonary disease

(*a*) *The Infective Agent* If laboratory tests were not taken at the onset failure to respond at 48 hr or evidence of deterioration indicate that such tests have become imperative and hospital admission is probably the wisest course If no local complication is evident treatment should be changed to one of the tetracyclines Chloramphenicol (Chloromycetin) should be used only on clear indication from the bacteriologist that the organism is most sensitive or sensitive only to it in view of the risk of blood dyscrasia Of the drugs available—chlortetracycline (Aureomycin) oxytetracycline (Terramycin) and tetracycline (Achromycin)—tetracycline has as wide a spectrum as any is tolerated better than most and serious side effects from it are less common A suitable dose is 0 5 g 6 hourly p c until the temperature has settled and then 0 25 g 6 hourly for 2 or 3 days Parenteral preparations are available for the severely ill or when vomiting is a feature

Where early bacteriological tests have been made the reason for failure of initial treatment may be evident and the appropriate drug must be substituted The pathogen may be cultured from the blood or in heavy growth from the sputum and its sensitivity to the range of antibiotics will be indicated Pathogenic pneumococci and haemolytic streptococci are virtually always sensitive to penicillin but penicillin resistant and insensitive staphylococci are on the increase Such organisms may be sensitive to tetracyclines but it may be necessary to seek an effective agent among the rapidly increasing range of antibiotics *e g* erythromycin oleandomycin novobiocin (Albamycin) not by haphazard trial but under laboratory guidance

Friedländer s bacillus is insensitive to penicillin and the drug of choice is streptomycin in large doses of 1 g 6 hourly reducing to 0 5 g 6 hourly for 3–4 days after the temperature has been normal for 48 hr Some strains are sensitive to tetracyclines



TUBERCULOUS EMPYEMA (R) COMPLICATING ARTIFICIAL PNEUMOTHORAX TREATMENT OF PULMONARY TUBERCULOSIS

Note the fluid level in the right pleural space and gross thickening of the visceral pleura



EMPHYSEMA

Note the voluminous thorax the hypertranslucent lung fields and the low flat diaphragm

Sputum tests should always include a search for *M tuberculosis* and if no other pathogen is isolated several examinations including cultures must be done as this organism is often difficult to find during the first 2 or 3 weeks of a tuberculous pneumonia If it is found treatment should begin with a combination of streptomycin 1 g i m daily and isonicotinic acid hydrazide 150 mg b d orally and admission to a suitable hospital be arranged The results of sputum examinations do not always explain the failure of routine treatment. Only the common commensals may be grown or a mixed flora with no particular pathogen predominating A possible virus aetiology must then be considered Some of the Psittacosis ornithosis group are sensitive to large doses of penicillin but in the absence of clinical response tetracycline may prove effective and should be given as outlined above

(*b*) *Complications of the Pneumonic Process* In spite of apparently adequate specific treatment the fever and toxaemia may continue or return after having settled for a few days In such event an empyema is suspected and should be sought by careful clinical examination and paracentesis in doubtful cases remembering that the signs are often atypical in children and in adults the condition may be undetectable clinically by virtue of its position or small size Expert radiography is then essential followed by needle exploration A serous effusion should be aspirated and most empyemas will respond to repeated aspiration and intrapleural penicillin Pulmonary suppuration and abscess formation may also prolong the illness and are considered below

(*c*) *Underlying Broncho pulmonary Disease* Complete or partial obstruction of a bronchus predisposes to and perpetuates infection distal to the block. The presence of stridor or a localized wheeze is suggestive and bronchoscopy should be performed Bronchial carcinoma is the commonest cause but foreign bodies stricture and extra bronchial pressure from neoplasms or hilar node enlargement must all be considered

In the majority of cases recovery will be complete in two or three weeks Resolution should be encouraged by postural drainage and breathing exercises and a further course of antibiotics if pathogens persist in the sputum Adequate convalescence is advisable and any case which has not run a straightforward course should be followed up by serial radiographs

PULMONARY SUPPURATION

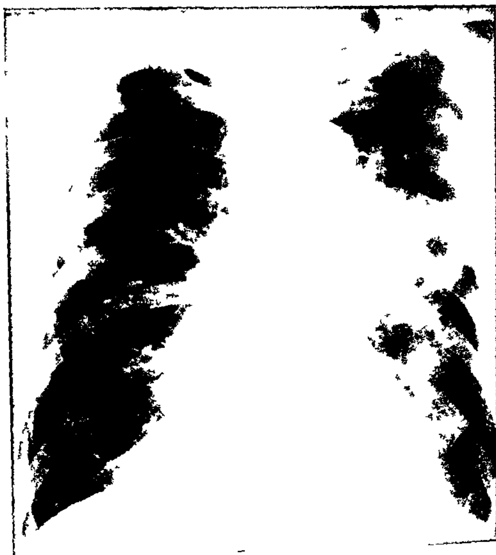
Lung Abscess Suppurative Pneumonia

Definition Pulmonary inflammation with the formation of pus within the lung

Aetiology Certain bacterial infections of the lung tend to progress to suppuration with the formation of single or multiple abscess cavities *Staph aureus* Friedlander s bacillus and actinomyces are examples of organisms capable of forming *specific lung abscesses* Septic embolism during a pyaemia or from an infected thrombophlebitis is another uncommon cause and such abscesses are usually multiple—*embolic abscesses* In the majority of cases however the primary event is bronchial occlusion by inhalation of infected material from the upper respiratory tract particularly at a time when the cough reflex and cilial action are depressed—*bronchogenic abscess* Initiating factors are therefore the same as those giving rise to localized aspiration pneumonia or infected atelectasis (*see* p 337) and whether or not suppuration ensues depends upon the virulence and type of the organisms in the aspirated material Predisposing factors are acute infections of the upper respiratory tract dental and gum sepsis operations on the nose and throat and post operative vomiting The septic material is more likely to be aspirated during deep sleep or while the cough reflex is depressed by anaesthesia cerebral vascular accident or by the influence of such depressant drugs as barbiturates morphine and alcohol

In addition to the above mechanism secretions may be retained beyond a bronchial obstruction and suppuration may follow Such abscesses not infrequently occur in association with bronchial carcinoma stricture bronchiectasis or a foreign body Occasionally also they arise as a result of infection of a lung cyst or by direct extension of a suppurative process below the diaphragm They may be called *secondary lung abscesses* Finally a malignant neoplasm in the lung may outgrow its blood supply so that its centre becomes necrotic and breaks down to form a *malignant lung abscess*

Bacteriology In the non specific forms of lung abscess a wide variety of organisms is found Frequently only normal commensals can be isolated and various pneumococci streptococci staphylococci Friedlander s bacillus and *H influenzae* are common the flora changing from time to time In some cases the predominant bacteria are anaerobic *e g* spirochaetes fusiform bacilli anaerobic streptococci and *B melaninogenicum* being similar to those found in patients with chronic gum infections Infection with such organisms is associated with a pronounced foetor (*putrid lung abscess*)



BRONCHIAL CARCINOMA

Note the mass extending out from the left hilum

an occasional complication of the more chronic cases as is also amyloid disease

Treatment. (a) *Preventive* Every precaution should be taken to avoid aspiration of infected material or blood clot during operations on the upper respiratory tract. Good oral hygiene should be encouraged and attained when possible before a general anaesthetic is given Prophylactic penicillin is advisable in circumstances where septic material might have been inhaled and bronchoscopy should be performed if a bronchial foreign body is a possibility

(b) *Curative* Conservative treatment with large doses of anti bacterial drugs and postural drainage should begin as soon as possible and should continue as long as clinical and radiological improvement are occurring Sputum examinations should be made to indicate the most suitable antibiotic but in general crystalline penicillin is the most effective and a dose of 2 000 000 units daily in divided doses is advisable The position of dependent drainage should be adopted for several hours daily and expectoration be assisted by vibrations and percussion of the chest along with encouragement to cough Regular sputum tests should be made as the bacterial flora may alter or become resistant and the addition of streptomycin or a change to tetracycline may become necessary

On this régime the clinical response is usually rapid and in favourable cases resolution is complete in 4–6 weeks Bronchography is advisable to assess the degree of residual bronchiectasis In more chronic or extensive cases medical treatment should continue to maximum improvement Pulmonary resection most commonly a lobectomy must then be considered in consultation with a thoracic surgeon Open drainage is now seldom employed.

During the course of the illness symptomatic treatment as for pneumonia may be required and the patient s general condition should be improved as far as possible by a nutritious diet rich in proteins and on occasions blood transfusion

TUBERCULOSIS

Tuberculosis is one of the oldest diseases known to afflict man Hippocrates gave an excellent description of it in its advanced stages 400 years B C. and named it phthisis (wasting) Since then it has been recognized in all civilized communities taking its toll of life especially among the poorer classes but not sparing the wealthy or the famous Throughout the ages little was learned of its nature or mode of spread until Villemin in 1865 stimulated by the work of Pasteur showed that tuberculous matter from an infected animal injected into another animal could produce the same disease The search for the causal organism went on until the tubercle bacillus was isolated by Koch in 1882

Incidence Soon after this momentous discovery pathologists began to report evidence of tuberculosis at post mortem in some 90 per cent of adults either pulmonary scars or calcified lymph nodes *but that the subjects had not died of the disease* The high incidence of infection in urban populations was soon to be confirmed by chest radiographs and tuberculin surveys and it became evident that the tubercle bacillus was ubiquitous but that infection by it by no means always led to clinical disease In this country to day *the incidence of infection* is approximately 40 per cent at school leaving age rising to 70 per cent at 20–21 years and to 80 per cent in middle age Thus infection is quite common but except perhaps when there is an overwhelming dose of bacilli the reaction of the tissues of the host is even more important in determining the development of the disease Since the latter part of the nineteenth century the overall mortality in this country has steadily declined from 60 000 per annum to under 5 000 the rate of decline being accelerated since the availability of effective anti bacterial drugs in 1946 Satisfactory as this seems it is offset by the notification figures which show that some 35 000 new cases are discovered each year

Bacteriology The tubercle bacillus (*Mycobacterium tuberculosis*) is a rod shaped aerobic non motile bacillus 0 5–4μ long and 0 3μ thick. It is acid and alcohol fast when stained red with Ziehl Neelsen s stain Different types are recognizable but for practical purposes only the human and bovine strains are pathogenic to man They can be differentiated by cultural features and animal inoculation but not by their clinical manifestations The human type is responsible for the majority of cases of pulmonary tuberculosis the bovine type being the more important cause of abdominal tuberculosis by virtue of its portal of entry Either type may be found in disseminated haematogenous lesions

Mode of Infection Much the commonest means of acquiring the infection is by *inhalation* of droplets of infected sputum from a victim of the disease Thus the majority of primary lesions are found in the lungs The infection may also follow *ingestion* of infected milk or rarely meat Occasionally *inoculation* through the skin occurs in laboratory

Morbid Anatomy The common sites for lung abscess are the posterior segments of the upper lobes and the apical segments of the lower lobes rather more commonly on the right side These are the areas to which inhaled material gravitates in the lateral and supine postures respectively The initial lesion is a segmental atelectasis due to bronchial obstruction by the inhaled material Consolidation follows and depending on the nature and virulence of the organisms varying degrees of necrosis and cavitation result In the more severe infections probably as a result of local vascular thrombosis part of the affected lung may become necrotic forming a slough within the abscess cavity which impairs drainage and delays healing An overlying pleurisy is always present The abscess may rupture into the bronchial tree and occasionally into the pleura If the infection is not checked the process may spread by further bronchial aspiration or directly across fissures producing irregular non segmental areas of suppuration (suppurative pneu monia) Extensive lung destruction may be produced in this way and even if healing eventually takes place much scarring and bronchial distortion will be left

Clinical Picture In many cases a careful history will reveal a recent operation on the upper respiratory tract *e g* dental extraction tonsillec tomy In others a period of unconsciousness may have occurred possibly with vomiting *e g* alcoholic stupor There is often a latent period of 1–3 weeks before symptoms arise In the absence of a clear story chronic gum infection and excessive tartar round the teeth are the commonest causes especially in patients already suffering from chronic bron chitis and emphysema in whom the cough may be ineffective The onset may be abrupt with rigor high temperature pleural pain and cough Sputum at first is scanty and mucoid but soon often sud denly a quantity of bloodstained pus is expector ated as the abscess discharges its contents into a bronchus In anaerobic infections this pus may be extremely foul smelling and tasting In other cases the sputum increases more gradually in amount and purulence with irregular haemoptyses Following expectoration of the abscess gradual improvement may take place spontaneously the sputum diminish ing and the fever subsiding but more commonly in untreated cases chronic suppuration continues with exacerbations of fever periodic haemoptyses and persistent cough which may produce several ounces of purulent sputum daily A leucocytosis is usually present The general health deteriorates quickly with progressive toxaemia clubbing of the fingers anaemia and loss of weight

Examination of the chest may reveal only a localized area of rales and weak breath sounds or the signs of consolidation A pleural rub may be heard at the onset The sputum in addition to the bacterial flora may contain pieces of necrotic lung tissue

Radiological examination may show an area of apparent consolidation but a cavity or cavities containing a fluid level with air above it and surrounded by a zone of consolidated lung is more commonly seen In progressive cases multiple areas of cavita tion are common within irregular areas of pneu monia Healing by fibrosis may taken place in some areas while the process continues to spread in others.

Diagnosis The specific types of lung abscess are recognized by isolation of the organisms from the blood or successive samples of sputum and in some cases by their characteristic radiographic appear ances In cases which have become chronic how ever superadded infection with a host of secondary invaders occurs and it is often impossible to dis tinguish them from the more common bronchogenic type

In the absence of a definite history or obvious predisposing factors the possibility that the abscess is secondary to organic bronchial obstruction par ticularly bronchial carcinoma should be considered. A slow or incomplete response to treatment also suggests this possibility Bronchoscopy may provide conclusive evidence but in cases where doubt persists thoracotomy may have to be advised Bronchiectasis may present a similar clinical picture but the history is usually of considerable duration Bronchography may assist in the diagnosis but since long standing lung suppuration may result in bronchiectasis the differentiation is seldom of great importance Dis tinction from pulmonary tuberculosis is not usually difficult provided the history is carefully considered and routine sputum examinations are made for acid fast bacilli Clubbing of the fingers and leucocytosis are not features of uncomplicated pulmonary tuber culosis but the radiological appearance may be very similar An empyema particularly if interlobar with a broncho pleural fistula may be impossible to distinguish from a lung abscess but the principles of treatment are essentially the same

Complications and Prognosis With prompt and energetic treatment the prognosis is favourable in most cases The outlook is necessarily worse in elderly patients or chronic bronchitics and in the more severe cases permanent lung destruction may remain Such patients are liable to recurrent chest infections unless the diseased area can be resected

Local complications include spread of the infec tion directly or via the bronchial tree to cause further abscesses or broncho pneumonia Empyema and pyopneumothorax are uncommon as pleural adhesions form early Cerebral metastatic abscess is

sensitive state can be produced only by living bacilli and affects all tissues but is most readily observed in the skin by means of the various tuberculin tests (*vide infra*) The evidence that hypersensitivity is accompanied by a partial immunity stimulated attempts at active immunization by avirulent organisms the most successful of which has been B C.G (Bacillus Calmette-Guérin) This vaccine contains a bovine strain of tubercle bacilli rendered avirulent by repeated subculture on special media Its aim is *to substitute* a *benign primary infection with attenu*ated bacilli for a naturally acquired and potentially dangerous primary infection An intradermal injection of 0 1 ml is given into the skin over the deltoid region This is followed by the development 3 weeks later of an indurated papule which may ulcerate Healing takes place after a period of weeks or sometimes months The tuberculin skin test should be repeated after an interval of 6 weeks and will have become positive in most cases If negative the vaccination is repeated Its persistence can be assured by repeating the skin test every year or two and if necessary re vaccination

Innate or Natural Resistance Much has still to be *learned of the factors influencing the natural* resistance to infection but some facts are known

1 *Influence of Race* With very few exceptions children are not born tuberculous the disease is acquired and just as different animals vary in their susceptibility to the disease so do the different races of mankind Primitive races such as the African negro have a poor resistance and rapidly progressive forms of the disease are common among them That this is not simply due to environmental and social factors is evident from the fact that members of the same race—the American negroes—living in good social circumstances show the same low resistance whereas the most impoverished and malnourished white does not. On the other hand, a race with a high resistance and low mortality rate is the Jew probably an effect of the process of natural selection rather than an inherent better resistance

2 *Influence of Age* The seriousness of the disease depends to some extent on the age at which infection is acquired (Table 16 1) The studies of Rich have shown that (*a*) tuberculosis is most fatal if acquired in the first year of life (*b*) it is much less dangerous but still serious from 1–5 years (*c*) a primary infection between 5 and 15 years is relatively benign and (*d*) that after puberty there is a sharp rise in mortality to a peak in the mid twenties

3 *Influence of Sex* Although tuberculin surveys show that the infection rate is the same for the two sexes the overall mortality is greater in the female between the ages of 15 and 30 years which is the period of active sexual life embracing puberty menstruation pregnancy and lactation and it seems probable that endocrine factors may therefore influence resistance to the disease Pregnancy itself *has not been shown to have a direct adverse affect,* but after delivery the added mental and physical stress disturbed nights and additional strain on a meagre family budget undoubtedly can

TABLE 16 1

Age in years	*Tuberculosis deaths per 100,000 estimated infected persons of each age period*
0–1	4 920
1–4	123
5–9	18
10–14	19
15–19	61
20–24	90
25–29	87

(Adapted from *The Pathogenesis of Tuberculosis* by A. Rich.)

4 *Influence of Social Conditions* There can be no doubt of the deleterious affects of malnutrition poverty overcrowding insanitary housing and overwork, and the tuberculosis rate is proportionate to their degree The incidence is still highest in the poorer classes of society and increases when social conditions decline still further as during times of war or economic slump

5 *Influence of Other Morbid Conditions* Certain other diseases seem to lower the resistance to tuberculosis *temporarily or permanently Measles diabetes* mellitus and silicosis are examples Exposure of the trunk to strong sunlight or ultra violet light may be followed by reactivation of quiescent pulmonary disease as may also the administration of steroids.

6 *Individual Immunity* Little is known about individual natural resistance and yet it is probable that herein lies the key to the understanding of the pathogenesis of the disease Even new born infants can resist and overcome infection with virulent organisms whereas there are a few cases reported of fatal progressive tuberculosis following vaccination with the avirulent organisms of the B C G type Although the disease itself is not hereditary it is probable that the capacity or otherwise to develop immunity is inherited

Tuberculin Skin Tests

The state of tissue hypersensitivity which develops about 6 weeks after tuberculous infection can be readily observed in the skin Koch s Old Tuberculin

workers or handlers of infected carcases and exceptionally rarely *congenital* cases result from transplacental spread

Pathology and Pathogenesis

Local Reactions to Tuberculous Infection At the site of invasion an inflammatory reaction occurs which is predominantly either exudative or productive in type The exudative reaction if in the lungs constitutes an area of tuberculous *pneumonia* the alveolar spaces being filled with inflammatory cells and plasma but with no actual destruction of lung tissue or replacement of it Complete reabsorption of such a lesion is possible with restoration of the normal architecture of the lung The productive reaction however is characterized by the formation of new tissue—tuberculous granulation tissue—comprising different types of cells young capillaries and its own reticulum which displaces and replaces the normal tissue The basic lesion of this granuloma is the "tubercle from which the disease derives its name It consists of—

1 A central group of epithelioid cells derived from the reticulo endothelial system
2 Langhans giant cells
3 a surrounding zone of lymphocytes and
4 a variable amount of fibrous tissue forming a partial or complete capsule

Under favourable circumstances the productive lesion may partially reabsorb leaving only a fibrous scar If it progresses however the tubercles coalesce to form macroscopic lesions and the centre undergoes a form of degeneration and coagulative necrosis known as caseation Caseous tissue consists of coagulated fat and protein and its formation in the host coincides with the development of a type of allergy known as tuberculin hypersensitivity In its turn the caseous material may become dehydrated and *calcified* or it may liquefy and be discharged from the surface of the body or into the lumen of an affected viscus In the lung this results in *cavitation* a momentous event in the development of the disease since the discharge of tuberculous material into the bronchial tree (*i e* the open case) sets the stage for progressive bronchogenic tuberculosis and renders the victim infectious to others The majority of cases of pulmonary tuberculosis pathologically are mixtures of exudative and productive reactions

At the same *time as these changes are taking* place at the primary site of invasion (the Ghon focus) the lymphatics draining the area become engorged and carry the infection to the neighbouring lymph nodes which undergo the same tissue reactions The *primary focus* and the lymph node component together constitute *the primary complex*

An active tuberculous lesion may invade the blood vessels giving rise to tuberculous bacillaemia. Alternatively a progressive primary infection may *spread up the lymphatic chain* the bacilli eventually reaching the blood stream via the thoracic duct. If large numbers of bacilli reach the blood stream disseminated miliary tuberculosis may result More commonly however haematogenous dissemination *produces small foci in many organs including the* lungs but they usually heal without causing clinical disease at the time In some cases however after a varying interval of months or years these foci may recrudesce Certain organs are more commonly the *site of these haematogenous lesions notably the* bones and joints kidneys adrenals the skin and the lungs In the lungs evidence of these early disseminated lesions can often be found soon after the primary infection They appear as small discrete *foci in the upper third of the lung fields* (Simon foci) In the majority of cases these absorb or heal and the apical scars or calcified spots so often seen in routine chest radiographs of adults are the end result Sometimes however these foci may later reactivate caseate and break down presenting the picture of adult bronchogenic phthisis (*endogenous re infection*) There is also plenty of evidence that repeated exposure to infection may initiate the adult type of the disease in patients who already have the partial protection afforded by a healed primary infection (*exogenous superinfection*) Which of these two modes of development of the disease is the more common has still to be decided

Tuberculin Hypersensitivity, Resistance and Immunity

Acquired Resistance Within a few we ks of the establishment of a tuberculous infection all the tissues of the body become hypersensitive to the products of the tubercle bacillus Koch first demonstrated this by animal experiment He *showed* that inoculation of tubercle bacilli into the skin of a previously uninfected animal produced no reaction for 10 days a nodule then formed which ulcerated and was accompanied by dissemination of the bacilli throughout the body On the other hand skin inoculation of an animal previously infected was followed by a prompt acute inflammatory response and ulceration but this healed quickly and the inflammatory reaction apparently served to localize the infection and prevent the v id spread dissemination of the bacilli Thus a state of hypersensitivity had been established and at the same time but not necessarily because of it the host had acquired some degree of resistance to the infection The hyper

has extended up the thoracic chain enlarged lymph nodes may be found above the clavicles

Diagnosis The tuberculin reaction is positive Tubercle bacilli can sometimes be cultured from the gastric contents or laryngeal swabs A radiograph of the chest may show the primary focus and enlarged lymph nodes but may fail to do so until many months or years later when calcification becomes evident

Complications and Sequelae In a few cases the infection may progress either locally in the com ponents of the primary complex or by blood stream dissemination

The *pulmonary component* may spread rapidly in an exudative form causing an acute tuberculous pneumonia Less commonly it may spread more slowly in the productive form cavitate and then progress as bronchogenic tuberculosis This is very rare in infants but not uncommon in adolescents Sometimes quite large hazy homogeneous shadows appear on the radiograph around the Ghon focus and may persist for months with little clinical dis turbance eventually clearing completely or leaving a few calcified spots Little is known of the patho logy of these perifocal infiltrations but they are thought to represent an allergic pneumonia due to diffusion of tuberculo protein into the tissues at the time hypersensitivity develops The term epituber culosis is applied to them and confusion may arise between them and segmental atelectasis from bronchial occlusion Involvement of the pleura with the formation of an effusion is rare in infants but is a common event in adolescent primary tuberculosis It tends to occur 3–7 months after the initial in fection Blood stream dissemination may produce isolated lesions in various organs or generalized miliary tuberculosis (*see below*)

The glandular component because of its size and the easy compressibility of the small bronchi of children may cause partial or complete bronchial occlusion On occasions a valvular obstruction may result with distension emphysema of the lobe or lung beyond More commonly however the ob struction is complete with segmental or lobar atelectasis distally Typical physical signs and X ray shadows may be evident Usually after a few months reaeration occurs as the glandular swelling subsides Sometimes when the bronchial wall has been invaded by tuberculous tissue rather than simply compressed the process of healing produces a stricture with persistent atelectasis This is not uncommon in the right middle lobe and is apt to be followed by bronchiectasis which may not declare itself until adult life A tuberculous lymph node may erode the bronchial wall and discharge its caseous contents into the lumen giving rise to tuberculous pneumonia Local spread of the infec tion may result in tuberculous pericarditis with effusion and subsequently constrictive pericarditis Recrudescence of infection in the mediastinal nodes may occur in later years and lead to cold abscesses presenting in varying sites around the chest wall If the infection is not arrested it may spread upwards through the mediastinal chain of lymph nodes to those at the root of the neck and may invade the blood stream via the thoracic duct

Blood stream dissemination occurs either by direct involvement of vessels in the primary focus or lymph nodes or via the lymphatics to the sub clavian vein Progressive tuberculosis of any organ may then result but there are certain organs more frequently involved in this haematogenous seeding *e g* bones and joints kidneys adrenals spleen and lungs Manifest disease may never appear at these sites but on the other hand may do so after a quiescent period of years Heavy blood stream in vasion by one of the routes already described is the cause of generalized miliary tuberculosis This is a possible complication of any active tuberculous in fection at any period of life but most cases occur in children within a few months of the primary infection

Treatment (*a*) *Preventive* This important aspect is discussed on p 352

(*b*) *Curative* Although most primary infections are benign any discovered should be kept under regular medical and X ray observation until resolu tion or calcification has occurred in view of its potential dangers and complications Efforts should be made to improve and maintain the general health by avoidance of fatigue adequate mixed diet gen eral hygienic measures and the early treatment of childhood infections The source of infection should be traced and any open case found in the household should be admitted to hospital for treatment Failing this the child should be admitted to a sanatorium

Treatment should be more strict in infants under 2 years of age and in cases showing progression of the disease Such patients require anti tuberculous drugs as described later Rest in bed should be con tinued until the temperature remains normal all signs of general illness have disappeared and the patient is gaining weight This may take some months to achieve and largely depending on the home situation it may be advisable to admit the child to a sanatorium where all facilities for treat ment nursing graded convalescence and education exist

Miliary Tuberculosis

Clinical Picture The com monly an infant or young cl

(O T) is a heat sterilized filtrate from glycerine broth cultures of tubercle bacilli concentrated to 1/10th of its volume This solution containing tuberculo protein is used in various dilutions for tuberculin skin testing A purer preparation from which the broth proteins have been removed is known as P P D (Purified Protein Derivative) and is preferred by some

Methods *Von Pirquet s Test* The skin of the volar aspect of the forearm is scarified through a drop of undiluted O T This test is no longer in use in this country

Mantoux Test An intradermal injection of 0 1 ml of 1 10 000 O T is given into the skin of the flexor aspect of the forearm and the result noted after 48–72 hr If no reaction occurs the test is repeated with 1 1 000 solution and if still negative with 1 100 A positive reaction is indicated by a raised indurated area of at least 0 5 cm in diameter at the puncture site with variable surrounding erythema This test is reliable and quantitative P P D may be used instead of O T and is available in two strengths the stronger being roughly equivalent to 1 100 O T

Heaf s Multiple puncture Test A spring loaded gun is used to make 6 punctures through the skin on which has been placed a drop of adrenalized O T or a solution of P P D containing 2 mg/ml *i e* equivalent to 100 000 units O T /ml The result is read after 72 hr the presence of induration around the puncture scars indicates a positive reaction + a ring of induration ++ a plaque of induration 0 5–1 cm in diameter +++ and a wheal of more than 1 cm diameter ++++

Vollmer Patch Test and Tuberculin Jelly Test These have the advantage that no skin puncture is needed and therefore appeal to young children In the former a prepared adhesive patch is used and in the latter the jelly is applied direct to the skin previously slightly roughened with sandpaper and covered with strapping for 48 hr It is then removed and the result is read after a further 24 hr A reddened infiltrated area corresponding to the site of application indicates a positive reaction but since these tests are less reliable than the Mantoux or Heaf tests their results should be accepted only if unequivocally positive

Significance of the Tuberculin Reaction A positive tuberculin test means simply that the individual has at some time been infected with tuberculosis It gives no indication of the activity of the disease and the test is therefore of comparatively little value in adults unless negative In infants however because of the time required for healing a positive test is strongly suggestive of recent or active tuberculous disease The degree of hypersensitivity affords no guide to the immunity of the subject but it does tend to parallel the acuteness of the infection except in its hyperacute forms *e g* miliary and meningeal tuberculosis in which hypersensitivity may fade Hypersensitivity may also fade as a result of measles and a negative skin test is also frequent in Boeck s sarcoidosis Hodgkins s disease and other reticuloses With these exceptions however a negative reaction virtually excludes active tuberculosis By means of tuberculin skin tests periodic surveys of the population can indicate the incidence of infection It is of value in helping to track down unsuspected sources of infection in closed communities and in the examination of child contacts of proven cases of the disease

Clinical Aspects of Primary Tuberculosis

Localization Since the disease is most commonly acquired by inhalation the usual site of the primary focus is in the lungs The intestine is the next most common site and rarely the tonsils larynx conjunctiva or skin The pulmonary lesion is a small focus of caseous pneumonia and may occur anywhere in the lung The lower part of the upper lobes and the upper part of the lower lobes are the commonest situation in children and the lesion itself is subpleural In adolescents the sub apical parts of the lungs are more commonly affected

Clinical Picture In the majority of cases the primary infection produces no detectable symptoms and both the pulmonary and glandular components heal by fibrosis and calcification without treatment and without having been recognized at the time In some cases however rather vagu symptoms such an anorexia over tiredness la k of energy slight fever and loss of weight are noted The development of allergy to tuberculo protein some 6–8 weeks after infection is sometimes accompanied by other allergic manifestations particularly *erythema nodosum* and *phlyctenular conjunctivitis* Although these conditions may have a varied aetiology their appearance in childhood or youth is nearly always indicative of primary tuberculous infection Cough is not a usual feature except in cases with considerable hilar node enlargement when it may be frequent and accompanied by stridor or wheezy dyspnoea sometimes confused with asthma These symptoms are referable to bronchial compression and distortion

Examination of the Chest In uncomplicated cases examination of the chest is usually negative but occasionally a localized wheeze may indicate bronchial narrowing D Espine s sign of whispering pectoriloquy audible over the 4th 5th and 6th dorsal spines is of no practical value If the infection

with an open case It differs from the primary dis ease in many respects The commonest sites for the lesions are the upper lobes and apices of the lower lobes caseation and cavitation are both common so that bronchogenic spread of the disease is a prominent feature on the other hand blood stream dissemination is rare hilar nodes are seldom de tectably enlarged the tissue response is usually a varied mixture of exudative and productive re- actions with evidence of healing by fibrosis and progression occurring at different sites at the same time In consequence the clinical picture is wide and varied but it is possible to classify the main types of the disease from their clinical or radiological features

Clinical Varieties

Acute Pulmonary Tuberculosis

(*a*) *Miliary Tuberculosis* This has already been considered *see* p 347

(*b*) *Tuberculous Pneumonia* (Plate **16.5**) The onset may be indistinguishable from the commoner types of bacterial pneumonia and the lung consoli dation may be of lobar or lobular extent Thus there may be a rigor pleural pain high fever cough and dyspnoea Sputum is scanty at first but is sometimes rusty or frankly blood stained Tox aemia increases rapidly with profuse sweating loss of weight swinging temperature and persistent tachycardia

The physical signs of consolidation can often be observed in the lobar type In the lobular variety scattered rales may be the only sign but patches of consolidation may also be detected The true nature of the disease is often first suggested by failure of an apparent case of coccal pneumonia to respond to routine treatment Tubercle bacilli are often difficult to find in the sputum during the first two or three weeks but eventually appear in large num bers as softening takes place

Chronic Pulmonary Tuberculosis

The disease may be acquired and progress to a considerable extent without producing symptoms of sufficient severity to lead the victim to seek advice It is not uncommon to discover the disease in an active form on routine radiography A small pro portion of such patients will admit to no symptoms even on direct interrogation but many will confess to minor symptoms previously attributed to such factors as extra work and worry a recent attack of influenza or smoker s cough On the other hand dramatic symptoms like pleural pain or haemop tysis can occur with a minimal lesion acuteness of symptoms does not necessarily parallel the extent of the disease

Clinical Picture The illness can present with symptoms of general toxaemia with chest symp- toms with symptoms referable to extra pulmonary complications or with combinations of these three groups

General Symptoms These are in no way specific as similar symptoms are produced by any chronic infective illness thyrotoxicosis and various psycho neuroses The onset is insidious with general lassi tude easy fatiguability and loss of weight. Dyspepsia and amenorrhoea are not uncommon A slight evening temperature may be noted possibly with some tachycardia and drenching night sweats which although not specific to this condition should always arouse suspicion

Chest Symptoms Any or all of the five cardinal symptoms of chest disease—cough sputum hae moptysis dyspnoea and chest pain—may occur Cough at first is slight but it persists and increases gradually to become productive as the disease ad vances Sputum at first is scanty and mucoid becoming mucopurulent and in later stages thick and purulent but odourless Haemoptysis is frequent and may be the first dramatic symptom it may amount to blood flecking or staining of the sputum the expectoration of small clots or frank haemor rhage of several ounces Chest pain may be typically pleural in type but perhaps more commonly rather vague pain described as an inconstant dull ache or an occasional stab is encountered Dyspnoea is not a prominent early feature but is usual as the disease progresses and where tuberculous bron chitis is present it may be wheezing in character

Various combinations of general and chest symp toms comprise the commonest form of presentation Occasionally extrapulmonary complications par ticularly tuberculous laryngitis enteritis ischio rectal abscess and genito urinary tuberculosis may lead to its recognition

General physical examination must be thorough in view of the several diagnostic possibilities raised by the symptoms and in order to detect metastatic tuberculous lesions The general condition and men tal outlook should be noted No particular physical type is especially prone to the disease The asthenic build or phthinoid type of older texts is more often the result of advanced or long standing dis- ease than a determining factor The majority of patients with early pulmonary tuberculosis present no obvious abnormal features on general inspection although there may be evidence of loss of weight Pallor malar flush slight cyanosis and clubbing of the fingers appear usually only in the late stages of the disease

to an open case of pulmonary tuberculosis may be discovered Adults are less often affected but surgical treatment of extrapulmonary tuberculous lesions may precipitate it

Unlike many septicaemias the onset is seldom abrupt It begins insidiously with *malaise head ache anorexia* and *fever* It is one of the causes of P U O the temperature may be *remittent or intermittent* and when charted may show *typus inversus* *i e* a higher reading in the morning than the evening There is usually no cough but *dyspnoea* and *cyanosis* may appear The general condition deteriorates steadily with *loss of weight* vomiting tachycardia drenching night sweats increasing drowsiness prostration and *coma* At any stage the symptoms and signs of meningitis may appear and dominate the picture

Fine rales and rhonchi may be heard scattered through both lungs but examination of the chest is often unhelpful The spleen is sometimes palpable and tubercles may be seen in the fundi If there is any sputum it may contain *M tuberculosis* The blood count is non specific and usually shows a slight leucocytosis and a secondary anaemia The tuberculin skin test is usually positive but may be negative in the fulminating case or terminally High quality radiographs of the chest will show the typical miliary mottling throughout both lung fields giving rise to a snowstorm appearance but it may not be detectable at the onset

Prognosis Prior to the discovery of streptomycin by Waksman in 1944 miliary tuberculosis was virtually always fatal in a matter of weeks or a few months An occasional patient survived for a year or two with the disease in a chronic miliary form and the exception eventually recovered The overall mortality with chemotherapy is now about 40 per cent but it is much less than this with early diagnosis and treatment

Treatment Hospital admission is necessary in order to obtain the requisite strict rest and nursing care which will be required for a long period This is vital in cases with meningeal involvement and such are best treated in special centres Specific treatment should begin at once and will need to be continued for many months after all evidence of activity of the disease has subsided Of the three most important anti tuberculous drugs streptomycin para aminosalicylic acid and isoniazid only isoniazid passes the blood brain barrier freely and it should therefore always be one of the combination of drugs given at the start in view of the risk of the development of meningitis It may be wise to give all three of these drugs together until the resistance of the organisms can be determined Streptomycin is given by daily intramuscular injection in a dose of 20 mg/kg body weight up to a maximum of 2 g Isoniazid is given orally in a dose of 10–20 mg/kg body weight usually 400 mg in divided doses The dose of sodium para amino salicylate is 0 5 g/kg body weight daily in divided doses to a maximum of 20 g in an adult If progress is satisfactory the dose of streptomycin is subsequently reduced to 1 g daily and thereafter combinations of the three drugs are continued as for pulmonary disease

Primary Tuberculosis in Adolescents

The steadily increasing effectiveness of preventive measures has reduced the incidence of primary tuberculous infection during the sheltered years of childhood and schooling so that 50–60 per cent of children of school leaving age have escaped infection Apart from other factors which may have a bearing opportunities for contact increase when these children go out into the world to earn a living and a significant proportion of them become infected during the next few years Although the primary complex forms in essentially the same manner in these adolescents certain differences should be noted Radiologically evidence of infection is often lacking the only evidence sometimes being the development of a positive tuberculin skin test in subjects under regular observation *e g* nurses and medical students in training Where the primary focus is visible radiologically it tends to be in the sub apical region The glandular component is much less obvious and complications attributable to bronchial obstruction are less common Although most primary infections in this age group heal just as they do in childhood a higher proportion of them tend to progress Pleurisy with effusion is much more common at this age and there is also a greater tendency for the primary focus to cavitate and present clinically as progressive bronchogenic tuberculosis indistinguishable from that of the adult type

Post primary Tuberculosis in Adults

(Re infection Tuberculosis Superinfection Tuberculosis Adult Phthisis)

In the present state of our knowledge of the pathogenesis of tuberculosis it must be inferred that progressive pulmonary tuberculosis as commonly seen in adults may arise either by recrudescence of post primary lesions acquired in the past or from a fresh infection by inhalation of bacilli from contact

single film it is often impossible to decide whether the disease is quiescent or active With experience however the diagnosis becomes one of strong probability and in the absence of further evidence serial radiographs provide the best means of decid ing whether the disease is progressing or not.

The value of tuberculin tests particularly in excluding tuberculosis has already been discussed The blood count is of little value as in most cases it is normal A slight anaemia is sometimes seen and in progressive disease the W B C may rise to 10 000–12 000/mm³ with a slight increase both in polymorphs and monocytes

Certain diagnosis depends upon the isolation of *M tuberculosis* from the respiratory tract secretions or pleural fluid In so far as other acid fast bacilli are occasionally encountered absolute proof rests upon successfully culturing the organism For prac tical purposes however if other evidence agrees the demonstration of acid fast bacilli by Ziehl Neelsen s technique or by fluorescent microscopy is sufficient for diagnosis. When available morning sputum is usually the material examined and if no bacilli are found in the stained smears the specimen can be concentrated centrifuged and examined again Inoculation of special culture media *e g* Löewen stein Jensen or Dubos Middlebrook media is a much more sensitive test but four to eight weeks must elapse before the result is known Similarly guinea pig inoculation gives no immediate informa tion and is more expensive The decision to treat a patient with anti bacterial drugs must often be taken before these results are available

Sputum may be absent or what there is may all be swallowed In such event laboratory examination can be made on resting gastric juice obtained by aspiration through a Ryle s tube first thing in the morning Alternatively laryngeal swabs may be taken by passing a moistened sterile swab into the upper part of the larynx on a bent wire This ex cites cough and infected droplets are caught by the swab which is then used for culture purposes Tracheal lavage is preferred by some 5 ml of sterile saline are injected rapidly down between the vocal cords and the material expectorated by the result ing violent cough is examined For the purpose of both laryngeal swabbing and tracheal lavage the examiner should wear a mask

Differential Diagnosis Many extrapulmonary diseases can give rise to general symptoms similar to those of pulmonary tuberculosis Important among them are thyrotoxicosis diabetes mellitus psychoneuroses and brucellosis A normal chest radiograph will serve to differentiate them as it also will patients with a chronic cough of bronchial origin but occasionally a patient is found to have two diseases *e g* diabetes and tuberculosis A great many pulmonary conditions give rise to cough sputum and an abnormal radiograph but in prac tice careful appraisal of the clinical picture a know ledge of the commoner radiographic appearances and repeated attempts to isolate the tubercle bacillus reduce the difficulties to comparatively few The *various forms of pneumonia* are distinguished by the absence of tubercle bacilli isolation of other pathogens response to chemotherapy rapidity of resolution and especially in children a negative tuberculin test *Lung abscess and bronchiectasis* are associated with purulent sputum which is negative for tubercle bacilli and the history may be distinc tive Other causes of lung cavitation and calcifica tion are not common in England but they are seen with the fungal infections *Histoplasmosis and Coc cidioidomycosis* which are not uncommon in the U S A Specific skin tests similar to the tuberculin test are available In the absence of proof of a tuberculous aetiology considerable difficulty may arise over a solitary round focus in adults since it may represent a tuberculous lesion a benign neo plasm a secondary deposit or a bronchial carci noma The removal of such a lesion and its subsequent histology may be the only means of differentiation Even more confusing are the occa sional cases in which an old tuberculous lesion is invaded by a new growth or suppurative pneumonia and in the process of lung necrosis tubercle bacilli appear in small numbers in the sputum Extensive bilateral pulmonary tuberculosis may produce a radiographic picture similar to a host of other con ditions *e g* occupational lung diseases sarcoidosis reticuloses carcinomatosis multiple infarction and chronic pulmonary congestion A careful history clinical examination and methodical investigation will usually provide the answer but sometimes only prolonged observation will decide it.

Classification Extent and Activity of the Disease. No satisfactory classification of pulmonary tuber culosis has yet been evolved to indicate the clinical *features extent and type of the disease and degree* of activity In Great Britain the Ministry of Health classification is based on the presence or absence of tubercle bacilli and the amount of constitutional disturbance In America cases are grouped accord ing to radiological type and extent into minimal moderately advanced and far advanced For the full details of these and other classifications larger works must be consulted

In clinical practice and particularly during treat ment recognition of active quiescent, and arrested disease is important. Activity of the dis ease may be obvious at the first examination or may be determined only after a period of observa

Clinical examination of the chest may reveal abnormal signs important when detected but it cannot be emphasized too strongly that *this examination is usually negative in early cases and may be negative in advanced disease* Even when signs are detected they may bear no relation to the extent of the disease It follows that in the presence of a suggestive history, a negative clinical examination is valueless as a means of excluding tuberculosis and a chest radiograph is essential Abnormal signs may however be found and in certain cases the stethoscope yields information which X rays cannot Inspection of the thorax may detect diminished movement over the affected area and localized wasting of muscles Palpation will confirm this and should be extended to exclude enlarged lymph nodes and signs of mediastinal displacement Percussion may elicit myotatic irritability over wasted muscles and an impaired note over the site of the lesion The most important sign detected by auscultation is the presence of a localized area of fine rales usually in the upper parts of the lungs and often only elicited immediately after coughing The classical signs of the various degrees of consolidation are occasionally observed and cavitation can only rarely be diagnosed with certainty clinically The disease in its different stages may be associated with a wide variety of pathological changes in the lung including infiltration consolidation cavitation atelectasis fibrosis bronchiectasis emphysema pneumothorax and pleural effusion The respective physical signs of these conditions therefore may all be observed in different cases at one time or another

Radiological Appearances The wide variety of lesions resulting from this disease is reflected in the equally varied radiological picture The interpretation of X ray shadows requires years of practice but the commoner types of pulmonary tuberculosis are as follows—

Tuberculous Pneumonia Radiologically this may be indistinguishable from other pneumonias in that a large area of lung sometimes of lobar extent becomes consolidated and opaque In a short time however cavitation tends to occur with the appearance of one or more translucent areas within the lesion

Infiltration This somewhat unsatisfactory term is commonly used to describe the early stages of the disease the appearance being of faint rounded but ill defined opacities most commonly in the upper zones Such infiltration is frequently unilateral but may be bilateral and if untreated tends to spread slowly down through the lung fields on both sides

Cavitation (Plate 16 6) Infiltrative lesions may coalesce to form irregular areas of consolidation which may then cavitate Such cavities appear as roughly circular or irregular translucent areas within an opacity itself often surrounded by further infiltration The size of the cavity varies from a few mm to several cm and a fluid level may be evident within it

Fibro caseous and Fibro cavernous Disease The fibrosis which occurs during the process of healing gives rise to streaky linear opacities and contraction of the affected segment or lobe of lung Lesions at different stages of development are commonly present in the same patient so that evidence of fibrosis may be seen in one part of the lung and more recent infiltration or consolidation in another (fibro caseous) Similarly extensive fibrosis and possibly calcification may be present with persistent cavitation (fibro cavernous)

Tuberculoma A not uncommon lesion is the solid round focus which is often solitary but may be multiple It casts on the radiograph a well defined circular opacity anything from a sixpence to a five shilling piece in size Small satellite lesions may be seen in close proximity and calcification is sometimes demonstrable within it Such lesions are often symptomless and discovered on routine radiography They represent a circumscribed area of tuberculous pneumonia a blocked cavity or a tuberculous abscess within an occluded bronchus

Calcification (Plate 16 7) Ultimate healing is often accompanied by calcification which because of its density is readily visible on radiographs The opacities are dense irregular and sharply defined and are usually accompanied by fibrosis of variable extent Such lesions are quite common on routine radiographs representing disease long healed and perhaps unrecognized On the other hand calcified lesions can co exist with active infiltration in other parts of the lung

Diagnostic Procedures Knowledge of the varied clinical picture together with an awareness that active tuberculosis may exist in a patient without complaints should lead to investigations whenever the slightest suspicion is aroused by the history A family history of the disease or contact with a sufferer may be discovered on direct interrogation and strengthens the need for a radiograph of the chest A previous pleural effusion recent influenza or disease known to be associated with pulmonary tuberculosis (*see* p 345) also provide important clues It bears repeating that a negative physical examination is insufficient to exclude this disease

Radiography of the chest is essential in any suspected case though even this examination cannot exclude tuberculosis in all cases Diagnosis cannot be made with certainty by this method alone since radiographs are but shadows furthermore on a

linen should be soaked in 1 20 carbolic for 12 hr before laundering

The control of tuberculosis is not purely a medical problem The incidence of the disease reflects the adverse effects of malnutrition over crowding poverty insanitary housing and a low standard of education Social and economic reforms must therefore advance with improvements in medical services Moreover integration of medical and social services is vital during after-care and rehabilitation

Curative Treatment

General Régime. All active cases of pulmonary tuberculosis require treatment of some kind or another and in most of them it will be necessary to inform the patient as gently as possible that he will be incapacitated for a period of 6–12 months Some patients can be treated successfully at home where conditions are suitable but the early stages of treatment are best carried out in hospital or sanatorium for several reasons In addition to nursing care hospital facilities enable a more complete assessment of each patient s disease to be made and his long term treatment can be planned and initiated during this time also he can be taught the precautions necessary to avoid infecting others and how to maintain his health once it has been regained

Pulmonary tuberculosis is a disease of infinitely varied natural history Untreated it may run a rapid downhill course to death in a few weeks it may heal completely leaving the patient well for the rest of his life it may heal and later break down or it may be a slowly progressive disease continuing for years Assessing the value of remedies for such a disease is extremely difficult, and conclusions derived from anything less than carefully-controlled studies with a prolonged follow up should be suspect, unless the remedy is so strikingly successful that all cases benefit as soon as it is given until the anti bacterial drugs there were no such remedies Collapse procedures were not applicable to all cases and much reliance was placed on various general measures including rest, high calorie diets and special climates As these were usually prescribed simultaneously the assessment of the relative merits of each one is even more difficult and controlled studies were hardly attempted

Climate is now regarded as unimportant, though extremes of temperature are undesirable and the atmosphere of the country is preferable to that of an industrial city where other respiratory infections are more prevalent. High altitudes are not suitable for those with extensive lung destruction and reduced respiratory reserve Exposure of the trunk to direct sunlight should be avoided in view of the risk of reactivation of the disease The added benefit given by the delightful resorts in Switzerland and elsewhere is largely psychological.

Bed rest is still important in the active stages of the disease Before any other treatment was available many patients even with cavitated disease recovered by rest, but the period required was usually many months and not infrequently years. Strict rest diminishes the oxygen demands of the body and adoption of the supine position reduces the lung volume by 20–30 per cent With the additional treatments now available there can be no doubt that the duration and strictness of the rest period can be very much modified but to what extent will not be fully determined for perhaps another decade It is unjustifiable to attempt the ambulatory treatment of active tuberculosis except as part of a carefully-controlled research programme Patients with predominantly unilateral disease should be advised to lie and sleep on the diseased side as this may afford some protection to the other lung A co-operative patient, by adopting the position in which the cavitated area is most dependent (postural retention") can sometimes achieve dramatic reduction in the size of the cavity Complete bed rest is necessary only with the severely ill febrile patient The use of a bedside commode is generally permissible as it involves less effort than the struggle with a bed pan Patients with minimal constitutional upset may be allowed up for toilet once a day Extension of activity beyond this depends on many factors but signs of improvement should have begun before the patient is allowed up for full toilet and perhaps one bath per week This degree of activity should not be increased until all signs of toxaemia have disappeared sputum conversion has been achieved and radiological evidence of regression and cavity closure is obtained The time required to reach this goal varies considerably but is seldom less than three months Gradually increasing amounts of exercise are then permitted beginning with half an hour up for each day for a week and increasing by perhaps an hour a day per week the rate of progress depending on the maintenance of maximum improvement.

Special diets have no proven value but it seems reasonable to give a high protein diet with the object of encouraging tissue repair Food fads should be discouraged extra vitamins are not necessary and the best way of persuading the patient to eat plentifully is to make the food appetizing

Anti bacterial Treatment (Chemotherapy) The comparatively recent introduction of specific anti bacterial drugs has revolutionized the treatment of

tion Thus chest symptoms with loss of weight and evening pyrexia coupled with an abnormal radio graph indicate activity and the need for treatment the demonstration of tubercle bacilli by one of the methods already described is a certain indication of activity as is also clear evidence of pulmonary cavitation in a patient hitherto untreated A raised E S R is supportive evidence only for activity may exist when this is normal The availability of a previous film may establish the fact that the lesion has appeared in recent months and activity can therefore be assumed Not infre quently a period of close observation is required during which cultures of sputum are made records are kept of evening temperature and weight and serial radiographs are taken for comparison Radio logical extension leaves no doubt as to the activity but a retrogressing lesion may also be active The important observation to make is whether it is a changing lesion or a stationary one

The disease may be regarded as quiescent when the following conditions have existed for six months the general condition and exercise tolerance should be satisfactory constitutional symptoms should be absent and repeated attempts to recover tubercle bacilli should have failed the radiograph should show no evidence of cavitation and the appearance of the lesion should be static or point to slow contraction When the disease has remained quiescent for a continuous period of at least two years it is permissible to refer to it as arrested. If no evidence of activity is discovered or when quiescence has been reached as a result of treatment a prolonged period of clinical and X ray observa tion is necessary in view of the possibility of relapse The case is reviewed every one to two months in the first instance the interval being gradually extended to three months for the first two years and thereafter at gradually increasing intervals The patient should be encouraged to attend at any time in between appointments should he suspect a re currence of symptoms

Treatment of Pulmonary Tuberculosis

Preventive Aspects

Pulmonary tuberculosis is an infectious disease notifiable to the Medical Officer of Health and as with any other infectious disease the first step in its control is detection of the source of infection For practical purposes this means an unceasing and co ordinated effort on the part of all branches of the medical profession and its ancillary services to discover open cases of the disease Such cases should be isolated until rendered non infectious by treat ment All contacts should be examined and kept under observation Skin testing is of particular value in the examination of child contacts and all positive reactors should be X rayed in addition Negative reactors should be offered the protection of B C G vaccination (which is comparable to that afforded by natural primary infection) Older children and adult contacts should have a chest radiograph and if contact is to continue this should be repeated at intervals Regardless of any immediate risk of con tact tuberculin negative children of school leaving age should receive B C G in view of the increased susceptibility at that age The same applies to young adults at increased risk *e g* medical students and nurses Submission to a medical examination in cluding a chest radiograph should be a condition of employment for teachers and others in close contact with groups of children

Unsuspected sources of infection to the extent of 4 per 1 000 X rayed have been disclosed by Mass Miniature Radiography Its use could be extended not only in closed communities such as schools and factories but to whole districts and even to the country as a whole the population being encour aged by education and propaganda to avail them selves of it

The eradication of bovine tuberculosis must ultimately depend on the extermination of all tuber culous cattle as has been largely achieved in some Scandinavian countries and in America In England this has not yet been economically possible Certi fied milk from T T herds is safe from the point of view of tuberculosis but carries no guarantee of freedom from other milk borne infections Pas teurization of milk has been a great advance but is not yet universally practised and much raw milk is still consumed in rural districts

The individual patient must be taught how to avoid infecting others and it is essential to obtain his co operation in these elementary precautions Ideally the positive sputum case should be isolated in hospital or sanatorium but this is not always pos sible If he must be at home he should have his own room from which children should be excluded and his own set of crockery which should be boiled and washed separately from the rest of the family Unnecessary cough should be discouraged and the mouth should always be covered during coughing Paper handkerchiefs and disposable sputum pots are ideal since they can be burnt after use Atten dants should all be Mantoux positive should wear gowns and masks during bed making and soiled

nantly fibrotic lesion anti bacterial treatment has less to offer but prolonged chemotherapy and rest sometimes produce striking results More often however a partial improvement with reduction in fever diminution and possibly conversion of sputum and gain in weight is achieved which enables surgical treatment to be performed with greater safety

The optimum duration of treatment with anti bacterial drugs is still a matter of opinion but in most cases a period of one to two years will be required whether or not additional treatment is employed

Several other antibiotics and bacteriostatic drugs are available but are either less potent or more toxic than the three already discussed Viomycin cycloserine oxytetracycline pyrazinamide and the thiosemicarbazones are examples to be borne in mind when confronted with a patient whose organisms have already become resistant to the usual remedies Gradually increasing doses of tuberculin in combination with anti bacterial drugs are still advocated by some for the more chronic type of lesion with indolent activity The value of steroids in suppressing drug reactions has already been discussed and the place of these compounds in combating tuberculous toxaemia and modifying the tissue response to the infection is being investigated The results are encouraging even in patients almost moribund but it is essential that chemotherapy should be given at the same time and that the bacilli should be drug sensitive

Collapse Therapy Until recently various measures were frequently employed to procure local relaxation of the diseased lung They are rapidly being abandoned as confidence increases in long term chemotherapy Occasionally however they are still required for recent or spreading infiltration not responding to anti tuberculous drugs possibly because of the presence of drug resistant organisms

Artificial Pneumothorax The introduction of air into the pleural space allows concentric relaxation of the lung and retraction of the diseased area provided the pleural surfaces are not adherent Pleural adhesions if not too extensive can be divided at thoracoscopy and the pneumothorax maintained by weekly refills of some 300–500 ml of air for a period of about three years Opinions vary as to the choice of suitable cases and the management of this form of treatment requires considerable experience It is applicable to patients with recent infiltration with or without some degree of cavitation and chiefly or entirely unilateral disease It is contraindicated for acute pneumonic disease predominantly fibrotic disease disease with extensive lung destruction or large peripheral cavities and in cases with evidence of tuberculous bronchitis In such it is either useless or fraught with danger

Phrenic Crush and Artificial Pneumoperitoneum Crushing the phrenic nerve temporarily paralyses the hemi diaphragm and allows it to rise some 2–4 cm Its effect lasts on an average six or nine months but is sometimes permanent especially in patients over 50 years of age It affords but a minor degree of lung relaxation and is therefore seldom used as the sole measure of collapse Combined with the introduction of air into the peritoneal cavity however the hemi-diaphragm will rise 2–4 in and can be maintained at this level by weekly refills of air Pneumoperitoneum is free of the pleural and pulmonary complications which can occur with pneumothorax and it can be applied to most forms of the disease It has little effect however on chronic cavities in the upper zone although it may help to control more recent spreads from such cavities and enable the patient to undergo thoracoplasty or resection at a later date

Thoracoplasty The grim prognosis of patients with unclosed cavities is well recognized and in the sphere of cavity closure surgery occupies an important place in treatment The modern thoracoplasty mobilizes the apex of the lung in the extra fascial plane and strips the lung off the mediastinum down to the hilum Properly performed it provides an excellent concentric relaxation of a diseased upper lobe which is then rendered permanent by removal of the upper ribs The operation is usually done in two or more stages and deformity is minimized by expert physiotherapy and limiting the operation when possible to resection of not more than five ribs Modifications of the operation are sometimes advised in order to achieve the same results in one stage and to avoid resection of ribs The space produced by the apicolysis is filled with a plomb in the form of plastic spheres or sponge Immediate results are good but late complications more frequent

Pulmonary Resection The concept of radical removal of the disease is attractive but it is important to realize that surgical excision can seldom eradicate the disease from the body Nevertheless resection can sometimes deal with a local part of the disease which could not be controlled by any other means It should be considered for the large round solid focus for patients with broncho stenosis and secondary infected bronchiectasis for the persistent lower lobe cavity and when a thoracoplasty has failed to achieve cavity closure It has been successfully employed for giant upper lobe cavities and areas of destroyed lung in various situations but the strongest arguments centre around its application to localized segmental lesions Increasing

pulmonary tuberculosis Properly applied they will arrest most tuberculous infections On questions of dosage duration of treatment and combinations of drugs opinions differ and change as further experience is gained but certain important principles have been established and will be stated

The three most important anti tuberculous drugs at present are *streptomycin para amino salicylic acid* and *isonicotinic acid hydrazide* Streptomycin derived from a soil actinomycete *Strep griseus* is given as the sulphate intramuscularly in a dose of 15 mg/lb of body weight to a maximum of 1 g daily Para amino salicylic acid (P A S) is given orally as the sodium salt the dose being 12–20 g daily Isonicotinic acid hydrazide (Isoniazid I N H) is given in tablet form by mouth 100–200 mg twice daily

Three factors govern the use of these drugs i e toxic effects of the drugs themselves the emergence of drug resistant strains of tubercle bacilli and the type of tuberculous disease

Toxic Effects Those of streptomycin are considered on p 38

P A S Serious side effects are rare but jaundice haematuria and albuminuria are occasionally seen Skin irritation rashes and drug fever are not rare and tend to appear in the second week of administration Anti histamines may control these hypersensitivity reactions but in severe cases the drug must be stopped When the symptoms have subsided desensitization should begin with 1 g or in severe cases 0 1 g daily increasing gradually until the normal dose is reached Nausea vomiting abdominal discomfort and diarrhoea are common and the most acceptable form of P A S must be found for each patient A simple unflavoured mixture after meals or following an alkaline powder is preferred by some but cachets granules and enteric-coated preparations are available

Isoniazid in the recommended dose is virtually non toxic Hyperexcitability tremor and difficulty in micturition are occasionally seen and usually respond to simple sedation Skin rashes including a pellagra like dermatitis and peripheral neuritis have been described particularly when doses in excess of 300 mg daily have been given In such cases pyridoxine 50–100 mg should be given concurrently

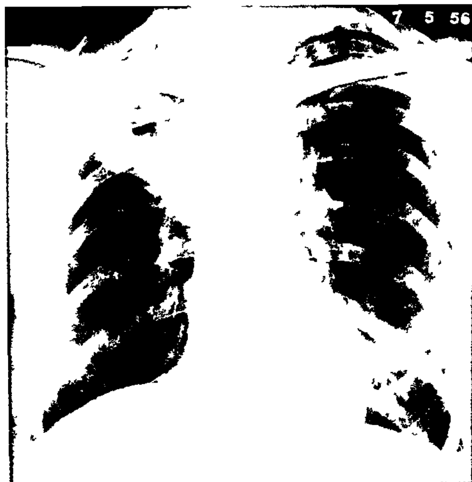
Recent experience suggests that when hypersensitivity reactions to these drugs are met the concurrent administration of steroids effectively suppresses the reactions and enables treatment to continue and even improves the rate of response to the drugs It is vitally important however that the infecting organisms should be drug sensitive

Drug Resistance In most untreated cases the majority of the bacterial population are sensitive to these agents A small proportion however are resistant to them and if any one of the drugs is used alone these resistant strains increase to the point of predominance after two to three months treatment in 60–80 per cent of cases This is particularly so in cavitated and confluent types of the disease This drug resistance should be avoided at all costs since it brings difficulties over and above the fact that the particular remedy is of no further value to that patient Deterioration is apt to follow and any new cases infected from such a patient will likewise be resistant Fortunately by giving any two of the drugs in combination not only is the therapeutic effect enhanced but also the emergence of resistant strains can be greatly delayed and to a large extent prevented It is a cardinal rule therefore that these drugs should never be given singly and in patients who have had previous chemotherapy sensitivity tests should always be made The administration of two of these drugs to a patient whose organisms are already resistant to one of the two is tantamount to giving the other drug alone In order to minimize the chances of resistance it is a wise plan to commence treatment of new cases with all three drugs until the sensitivities of the organisms are known Treatment should begin with streptomycin 1 g sodium P A S 12 g and isoniazid 200 mg daily In patients over 50 years of age the streptomycin may be given three times weekly to lessen the risk of eighth nerve damage to which they are more prone Thereafter recommended combinations are as follows

1 Streptomycin 1 g and isoniazid 200 mg daily
2 Streptomycin 1 g and sodium P A S 12–20 g daily
3 Sodium P A S 12–20 g and isoniazid 200 mg daily

Intermittent streptomycin and either daily isoniazid or sodium P A S is not recommended For Out Patient continuation treatment the most convenient combination is No 3 (above) as the drugs can be taken together in cachets orally in two equally divided doses

Type of Disease All cases of active tuberculosis will benefit from anti tuberculous drugs In early cases and in the acute forms of the disease—miliary pneumonic and acute bronchogenic forms including recent spreads from more chronic lesions—the effect is undoubted and frequently dramatic Pulmonary cavities especially if recent often close and with prolonged treatment frequently remain closed Tuberculous laryngitis and tracheo bronchitis respond rapidly and well For the long standing chronic cavitated type of disease and the predomi



BRONCHIAL CARCINOMA

There is atelectasis of the right upper lobe which contains a large abscess cavity The trachea is displaced to the right Bronchoscopy showed a neoplasm occluding the right upper lobe bronchus

evidence of the achievements of long term chemo therapy is curbing enthusiasm in this direction

Symptomatic Treatment In most cases treatment of individual symptoms is not required but it may be necessary occasionally for the following—

Cough Unproductive cough is undesirable and should be suppressed Simple advice to the patient to avoid coughing unless it is necesary to raise sputum coupled with abstinence from or drastic reduction in smoking is usually all that is required A simple linctus is sometimes required to allay the dry cough which is disturbing rest and sleep

Anorexia The appetite improves with the abatement of toxaemia and seldom needs stimulation A simple bitter before meals can be tried and some still advocate insulin before meals Most patients on isoniazid however quickly regain their appetite and no other treatment is required

Pain Pleural pain may occur at various stages of the disease Local heat strapping the chest in expiration analgesics and occasionally local anaesthesia may be used for its alleviation

Boredom Although not direct symptoms boredom and a general impatience with the enforced inactivity are commonly experienced and some patients will discharge themselves against medical advice unless these factors are understood and counteracted Various handicrafts and hobbies can be practised in bed and during the period of grading In all tuberculosis hospitals a good library and an occupational therapy department are essential ancillary services

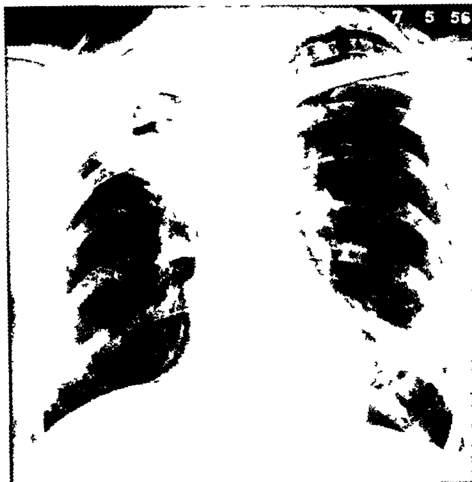
Haemoptysis Blood flecking or staining of the sputum is common and requires no treatment *per se* other than reassurance When several ounces of blood are expectorated the patient s anxiety should be allayed by a harmless sedative such as chloral hydrate or potassium bromide and he should be propped up on pillows in order to assist coughing If it is known which side the blood is coming from he should be inclined to that side to minimize the risk of soiling the other lung When the immediate bleeding has ceased he should lie for a few hours in the position of postural drainage the object being to remove blood which might transfer infection to other parts of the lungs For the same reason morphia and other cough suppressant drugs should be withheld except in the most severe cases Massive haemorrhage a rare event but sometimes fatal calls for morphia and a blood transfusion If it continues the induction of a pneumoperitoneum should be tried or the possibility of immediate lung resection must be considered

Prognosis With skilled treatment the immediate prognosis in early and moderately advanced cases is good and with the patient s full co operation the disease can be arrested in most cases Ultimate healing takes a long time and recrudescence may occur under a wide variety of circumstances already discussed as affecting resistance to this disease Approximately 10 per cent are destined to relapse some without any obvious cause and it is essential that regular observation should continue for several years in all cases as it is impossible to predict which patients will relapse In advanced cases the outlook is less favourable With prolonged treatment a stage of quiescence may be reached but some degree of disability will remain Under good social circumstances or in a Village Settlement such patients may live for many years in comparatively good health within their restricted capacities

Complications *Tuberculous Laryngitis* The larynx may become infected by direct implantation of bacilli in patients with a positive sputum The vocal cords arytenoids and epiglottis are the common sites of ulceration and hoarseness is the first symptom In advanced cases severe pain and dysphagia are features but fortunately this condition responds well to anti tuberculous drugs

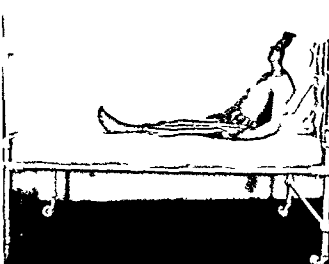
Tracheo bronchitis Infection of the smaller bronchi and bronchioles is common in the diseased area particularly in relation to cavitated disease In some cases however the trachea and large bronchi are involved Diagnosis rests upon bronchoscopic examination but the condition may be suspected clinically in the presence of severe cough and dyspnoea out of proportion to the extent of lung involvement wheeziness sometimes with a localized rhonchus and a heavily positive sputum in the absence of demonstrable cavitation The tuberculous bronchitis itself responds well to anti bacterial treatment but in the process of healing broncho stenosis is not uncommon This condition is important because of the risk of pulmonary atelectasis which may adversely affect the course of the disease and modify the choice of treatment

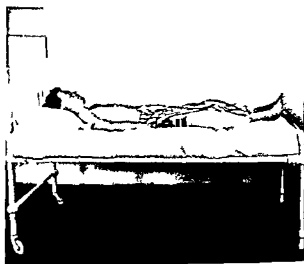
Pleural Complications Dry pleurisy is a common complication during the active stages of the disease A pleural effusion may also appear at any time but is most common in young adults soon after the primary infection (*see* p 362) Spontaneous pneumothorax is an occasional complication most cases of this condition being non tuberculous in origin The gross soiling of the pleura which follows rupture of a tuberculous cavity or pleural adhesions may give rise to a *tuberculous empyema* or *pyopneumothorax* Before adequate chemotherapy was available this was a dreaded complication of pneumothorax treatment especially after adhesion section Instillation of streptomycin and thorough aspiration is required to obliterate the pleural space by re expansion of the lung but in neglected or chronic

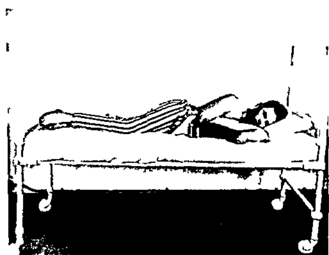


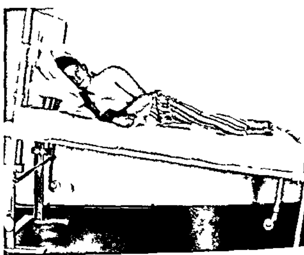
BRONCHIAL CARCINOMA

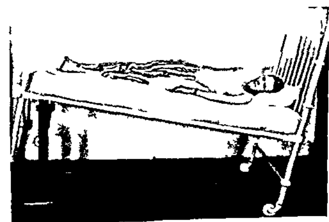
There is atelectasis of the right upper lobe which contains a large abscess cavity. The trachea is displaced to the right. Bronchoscopy showed a neoplasm occluding the right upper lobe bronchus.


(a)


(b)


(c)


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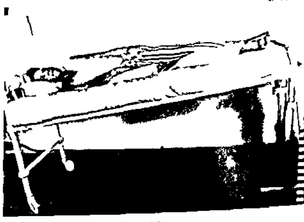
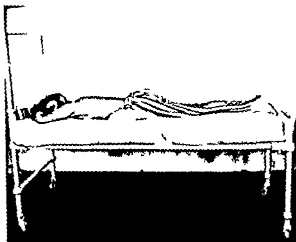
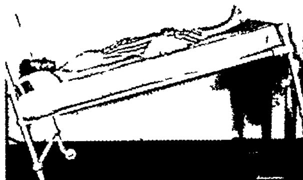

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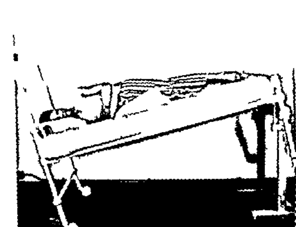
PLATE 16 12



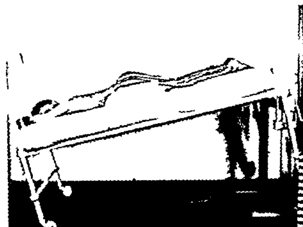
(g)



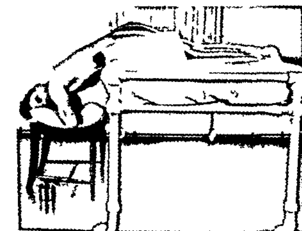
(h)



(i)



(j)



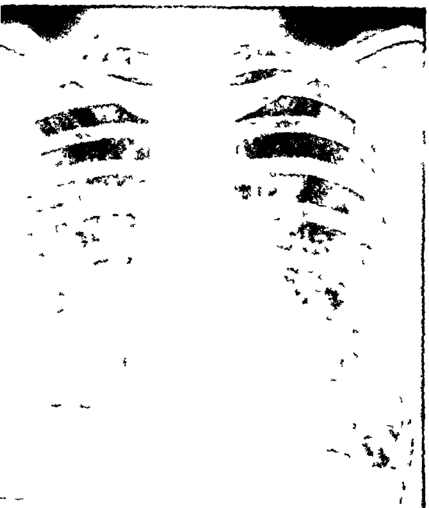
(k)

PLATE 16 13

POSTURAL DRAINAGE OF THE LUNGS

(The illustrations should b studied in conjunction with the diagrams in Fig 16 1)

(a) Apical segment of upper lobe(s)
(b) Anterior segment of upper lobe(s)
(c) Posterior segment of right upper lobe horizontal half prone position with supporting pillows for head and trunk
(d) Posterior segment of left upper lobe Half prone position with 9 in elevation of trunk by pillows or blocks under head of the bed
(e) Right middle lobe 45 rotation to the left with the foot of the bed raised 12 in
(f) Lingula segments of left upper lobe 45 rotation to the right with the foot of the bed raised 12 in
(g) Apical segment of lower lobe(s) horizontal position with pillow under the abdomen
(h) Anterior basal segment of lower lobe(s) tipping angle 45 approximately
(i) Lateral basal segment of lower lobe tipping angle 45 approximately (For the right lateral basal segment the patient lies on the left side)
(j) Posterior basal segment of lower lobe(s) tipping angle 45 approximately
(k) Alternative position for drainage of posterior basal segment of lower lobe(s) more readily adaptable in the home



MULTIPLE METASTASES IN THE LUNGS FROM MELANOTIC SARCOMA

SUPERIOR VENA CAVAL OBSTRUCTION

Note the bloated face the swollen arms and engorged veins The patient had bronchial carcinoma with metastases in the mediastinal lymph nodes

PLATE 16 14

cases when considerable pleural thickening has occurred excision of the empyema possibly with resection of the diseased area of lung is the most satisfactory treatment.

Blood stream Dissemination This has already been described and is distinctly uncommon in the adult type of the disease except in advanced cases

Tuberculous Enteritis Ulceration of the lower ileum and caecum may develop in patients as a result of swallowing large quantities of sputum containing tubercle bacilli General abdominal discomfort with repeated colic and diarrhoea are the usual symptoms The general condition deteriorates rapidly with loss of weight and anorexia It is usually a complication of advanced disease but may respond to anti bacterial treatment

Ischiorectal abscess and anal fistula may be the first lesions to arouse suspicion of pulmonary tuberculosis A proportion of these abscesses are initially tuberculous They occur in patients with little or no sputum and the route of infection is a matter for conjecture It is important however to advise a chest radiograph for any patient presenting with such a lesion

After-care and Rehabilitation

The aim of treatment is not only to arrest the disease but to restore the patient s working capacity if possible in the employment for which he has previously been trained provided it is suitable During the convalescent stage in the sanatorium favourable cases will have reached the point of being up all day and performing light manual work The suitability of previous employment should be considered during this time and if necessary arrangements for training for more suitable work can be made The patient s working capacity is likely to be limited for a considerable period and sheltered employment can be obtained by registering him as a disabled person under the Disabled Persons Act of 1944 For the permanently incapacitated infectious case able to do a restricted amount of work but unable to compete on equal terms with others the Village Settlement is most suitable The whole family is cared for in the settlement and the patient receives a subsidized wage for his limited hours of work

Regular attendance at a chest clinic or hospital for observation is particularly important in order to detect early the few patients who will relapse A chest radiograph will be required at least three monthly for the first two years the interval then being gradually extended to six months and finally a year Personal and social problems will require discussion and advice and the assistance of Almoners Health Visitors and Welfare Workers should be freely available Marriage and pregnancy are best postponed until the disease has been stable under ordinary living conditions for at least two years Decisions on these important aspects however can be taken only after a frank discussion of the wishes and economic state of the couple concerned. Pregnancy itself seldom affects the disease adversely but after delivery the extra work and anxiety disturbed nights and added strain on a meagre family budget may do so If termination is advised it should be carried out during the first three months Breast feeding should be avoided if the mother has open tuberculosis or whenever doubt exists as to the quiescence of the disease Infants born of tuberculous mothers should preferably be separated at once and receive B C G vaccination They should not return to the mother s care until they have achieved Mantoux conver ion and her disease is quiescent

PULMONARY EMPHYSEMA

Definition The term emphysema describes several conditions in which there is local or generalized abnormal inflation of the lungs with air which cannot be readily expelled

Types of Emphysema

Acute Obstructive Emphysema

Simple generalized over inflation of the lungs is observed during an acute attack of asthma and is a temporary phenomenon unaccompanied by structural changes in the alveoli In long standing cases however the chronic obstructive type supervenes (*see below*) Localized obstructive emphysema is uncommon but results from partial obstruction of a bronchus by such conditions as foreign body enlarged hilar nodes or bronchial neoplasms A check valve mechanism is produced which permits air to enter and distend the affected segment lobe or lung but prevents its free expulsion A localized wheeze may be heard with the stethoscope breath sounds and movement are decreased and the mediastinum may be displaced to the opposite side An area of increased translucency is seen on radiographs or on radioscopy particularly in expiration Its detection indicates the need for further investigation particularly by bronchoscopy

Compensatory Emphysema

Reduction in volume of part of the lung by atelectasis cicatricial contraction or pulmonary resection is accompanied or followed by over distension of surrounding segments If moderate in degree this is of no clinical significance but severe over inflation may impair pulmonary efficiency In coal miner s pneumoconiosis the alveoli round the multiple dust foci are dilated giving a honeycomb appearance to which the term *focal emphysema* is applied.

Atrophic or Senile Emphysema

Atrophy and degeneration of the alveolar walls is seen in old age and the total volume of the lungs is reduced It is part of the general process of ageing but seldom causes dyspnoea in view of the diminshed activity requirements of those in advanced years

Bullous Emphysema

Superficial blebs or bullae are common in association with chronic obstructive emphysema In some cases however solitary or multiple air containing cysts are seen in patients with no evidence of generalized expiratory obstruction It is presumed that such cysts which may increase to giant proportions arise by a valvular mechanism at bronchiolar level possibly induced by scar tissue from antecedent pulmonary disease

Interstitial Emphysema

Rupture of alveoli or bronchi may permit air to escape into the interstitial tissues of the lung Following chest injuries or operations or sometimes during severe bouts of coughing or straining against a closed glottis such injuries may be sustained The air tends to track along the peribronchial and perivascular sheaths into the mediastinum (*mediastinal emphysema*) and then up into the subcutaneous tissues of the neck face arms and trunk where it becomes palpable as *surgical emphysema* Retrosternal pain or tightness and dyspnoea may be mild or severe according to the volume of air and pressure in the mediastinum Rarely obstructive symptoms and signs develop Not uncommonly the mediastinal or visceral pleura may rupture and cause a pneumothorax The presence of air in the mediastinum gives rise to crunching or crackling sounds readily audible on auscultation over the cardiac area especially during systole and diagnosis can usually be confirmed by radiography particularly in the lateral views Treatment other than rest is seldom required and recovery is the rule Exceptionally if mediastinal pressure symptoms are severe a catheter may be inserted into the superior mediastinum through an incision in the suprasternal notch to allow the air to escape

Chronic Generalized Obstructive Emphysema (Hypertrophic Emphysema)

This is the important and common type of emphysema characterized by generalized permanent over inflation of the lungs with disruption of alveolar walls and diminished elasticity

Aetiology The exact cause is incompletely understood but certain factors seem to play an important part In the great majority of patients there is a history of chronic bronchitis or asthma of some years duration Occasionally however no such history is obtained or at the most the main symptom of dyspnoea dates from an isolated respiratory infection Probably diffuse bronchiolar obstruction itself a consequence of inflammation is the main underlying lesion When complete this results in lobular atelectasis and compensatory emphysema around when incomplete air may enter the distal alveoli in inspiration but be retained in expiration and the persistence of this distending force ultimately leads to rupture and degeneration of the alveolar walls with a diminution in elasticity and obliteration of lung capillaries Chronic cough doubtless enhances these factors and increases the rate of development of emphysema It is also possible that a constitutional weakness of elastic tissue predisposes to the condition since not all chronic bronchitics develop this disease

Morbid Anatomy The lungs are voluminous and pale and fail to collapse when the pleura is opened at autopsy The surface may be indented by the ribs and show numerous blebs or bullae Histologically the changes of chronic bronchitis and bronchiolitis are usually evident There is patchy dilatation of alveoli particularly in the cortical parts of the lungs with thinning and in places rupture of alveolar walls to form large air spaces of variable size some of them visible macroscopically as bullae

Effect of Emphysema on Respiratory Function Consequent upon diffuse obstruction to expiration there is a considerable increase in the volume of air left in the lungs at the end of both normal expiration (functional residual volume) and after maximal expiration (residual volume) The ratio of residual volume to total lung volume normally 30 per cent is always increased Inspired air is therefore subjected to greater dilution The vital capacity is diminished but is an unreliable index of the degree of emphysema unless the time taken for expiration is considered The normal person can expire 80 per cent of his vital capacity in one second an emphysematous patient may expire the

same proportion of his vital capacity by conscious effort but takes much longer to do so For similar reasons the maximum breathing capacity is always reduced The diminished elasticity of the lung is reflected by a less negative intrapleural pressure i e it approaches nearer to atmospheric pressure and indeed may reach atmospheric pressure and even exceed it at the end of expiration Unfortunately increasing the efficiency of expiration by voluntary effort can help in emptying the lungs only to a limited extent because when the intrathoracic pressure reaches a certain level the diseased bronchioles are themselves shut down and air is trapped distally The patchy distribution of alveolar disruption and bulla formation also result in uneven distribution of inspired air relatively more going to the more readily distended and avascular spaces Thus a pathological dead space is created with considerable impairment of pulmonary ventilation The eventual effects of this inadequate ventilation are diminution of the oxygen saturation and an increase in the carbon dioxide content of the arterial blood at first on effort and later even at rest The respiratory centre becomes relatively insensitive to carbon dioxide and respiration is maintained largely by anoxic reflexes from the aortic and carotid bodies Chronic anoxia often induces a secondary polycythaemia of the order of 6 000 000 to 6,500 000 R.B C /mm³ with increased blood viscosity Ultimately the summation of all these effects leads to pulmonary hypertension right heart stress and hypertrophy and cardiac failure (Cor pulmonale) most commonly precipitated by an acute respiratory infection

Clinical Picture No age is immune but the commonest age at onset is 40-50 years and men are more frequently affected than women The outstanding symptom is dyspnoea It is insidious in onset appearing only on severe effort in the first place but gradually increasing until it is provoked by slight exertion or in advanced cases even present at rest It tends to improve during the warm dry weather and increase in the damp cold and foggy winter months This doubtless corresponds with the chronic bronchitis from which most patients suffer The great majority of patients give a history of bronchitis or asthma for a number of years but occasional patients are seen with no such history or who date the dyspnoea from an isolated respiratory infection The rate of deterioration varies considerably In some cases the breathlessness increases very slightly over a period of twenty years or more while others may be severely incapacitated within a year or two Chronic cough sputum and wheezing are present in most cases attributable to the associated bronchitis

Physical signs in the established case are diagnostic There may be cyanosis detectable most readily in the nail beds which themselves may show some degree of clubbing The accessory muscles of respiration are in action and filling of the cervical veins towards the end of expiration is commonly seen as the intrapleural pressure rises The chest is held in a position approximating full inspiration the shoulders are raised the antero posterior diameter of the chest is increased the subcostal angle obtuse and there is some kyphosis Emphysema may however exist without such deformity The chest is rigid and expansion following maximum expiration seldom exceeds one inch The lower ribs and intercostal spaces may be drawn in during inspiration (paradoxical respiration) owing to the low position of the diaphragm its effective force being then in a horizontal direction Palpation confirms the poor movements and vocal fremitus is diminished generally The apex beat is usually impalpable through the chest wall but often visible in the epigastrium The percussion note is hyperresonant and the normal areas of dullness are obliterated in varying degree The breath sounds are usually weak and vesicular with shortened inspiration and prolonged expiration The heart sounds are faint, sometimes inaudible but can best be heard in the epigastrium Scattered rales and rhonchi are commonly present as indications of the associated bronchitis

Radiography of the chest shows a voluminous thorax with increased transradiancy of the lungs The ribs are more horizontal and the intercostal spaces widened the diaphragm is low in position flattened and moves little on radioscopy The normal vascular shadows may be sparse in the outer lung fields but the hilar shadows are relatively prominent Bullae may be seen which show comparatively little change on inspiratory and expiratory films (Plate 16 8)

Diagnosis Advanced cases present little difficulty Other pulmonary diseases causing dyspnoea are excluded by radiological examination In early or doubtful cases however pulmonary function tests provide the most reliable evidence of emphysema by demonstrating the relative increase in residual volume the inefficient mixing of gases and the impaired ventilation

Course and Complications By the time emphysema produces symptoms irreversible changes have occurred in the lungs It tends to progress slowly year by year but its progress can be retarded or even arrested for a considerable period with treatment Its course may be punctuated by spontaneous pneumothorax which is sometimes bilateral The diminished respiratory reserve increases the hazard

of chest infections which are not infrequently complicated by pulmonary atelectasis or bronchiectasis because of the ineffective cough Patients who survive the frequent exacerbations of bronchitis may ultimately succumb to cardiac or respiratory failure

Treatment *Preventive* The problem is essentially the same as that discussed under chronic bronchitis p 322 In essence however it is most important to remove sources of bronchial irritation to counteract bronchospasm and to treat respiratory infections early This involves guidance in the choice of occupation and place of residence strict avoidance of tobacco and the effective use of anti spasmodics and antibiotics

Symptomatic Important as it is in the prevention of emphysema the control of bronchial irritation is essential in patients already showing symptoms and signs of the established disease There should be no compromise about stopping smoking Measures for the relief of chronic bronchitis and bronchospasm should be instituted as described fully on p 322 and any acute exacerbation of respiratory infection should be treated energetically with appropriate antibiotics Improved diaphragmatic function may be achieved by physiotherapy with emphasis always on the expiratory phase of respiration and conscious control of the abdominal muscles (*see* p 385) Efforts to raise the level of the diaphragm and so place it in a position of greater function by such measures as raising the foot of the bed or wearing a tight abdominal binder may help some patients The induction and maintenance of a pneumoperitoneum is also advocated by some but is badly tolerated by the severely incapacitated patient who is in the greatest need of assistance Surgical measures have a limited scope Local resection of large bullae or emphysematous segments occasionally helps the dyspnoea by allowing better ventilation of more normal lung and denervation of the lung at the hilum sometimes relieves chronic bronchospasm The application of these procedures is not yet fully defined

Respiratory Failure

A variety of conditions including organic nervous disorders of the brain stem drug intoxication and paralysis of respiratory muscles can produce respiratory failure but it is considered here because advanced emphysema is the commonest cause In such patients it is frequently precipitated by an acute chest infection or exacerbation of coexisting bronchitis The impaired ventilatory capacity permits the alveolar pCO_2 to rise and the pO_2 to fall below normal As a result anoxaemia, hypercapnia and acidaemia develop and may have serious effects upon the cerebral and pulmonary circulations The cerebral vessels dilate and the C S F pressure rises, papilloedema and retinal haemorrhages are sometimes observed Throbbing headache and mental confusion are common symptoms and hallucinations delusions increasing stupor and finally coma may follow Coarse twitching of the limbs and face and profuse sweating are additional signs which should suggest the clinical diagnosis of respiratory failure without waiting for the confirmation obtained by blood gas analysis The peripheral vessels also undergo vasodilatation Although the nail beds may be cyanosed the hands are warm, the digital vessels throbbing and the pulse of increased volume On the other hand the pulmonary arterioles are constricted and the pulmonary artery pressure increases This additional burden on the right ventricle may precipitate right heart failure

Treatment The essentials are (*a*) appropriate antibiotics to combat the infection (*b*) the administration of bronchodilators and the encouragement of expectoration and (*c*) oxygen Tetracycline 500 mg 6 hourly or a combination of penicillin 1 000 000 units and streptomycin 1 g i m b d are effective modifications being made according to the bacterial flora of the sputum Frequent inhalations of 1 per cent isoprenaline combined with a detergent aerosol *e g* Alevaire are helpful and during the acute stage aminophylline 0 25–0 5 g i v b or t d s is most valuable Nikethamide 5–10 ml i.v 4–6 hourly will stimulate cough and expectoration in stuporose patients and amiphenazole 150 mg i v is a reliable respiratory stimulant. Postural drainage is instituted as soon as it can be tolerated but in severe cases frequent aspiration of thick sputum by blind intubation or through a temporary tracheostomy may be justified Tracheostomy is often life saving as it enables aspiration of bronchial secretions to be performed frequently and improves oxygenation by reducing the volume of the dead space Oxygen can easily be given through the tube and if necessary adequate pulmonary ventilation can be maintained through it by means of an artificial respirator Response to steroids is unpredictable but where the previous history has been predominantly that of asthma they are sometimes dramatic in their effects The administration of oxygen although essential requires caution It has already been noted that in this condition the respiratory centre is relatively insensitive to carbon dioxide and that breathing is largely maintained by anoxic reflexes. The rapid removal of anoxia by oxygen administration may be followed by further depression of respiration and even complete cessation with exaggeration of the symptoms and signs of respiratory failure High concentrations of oxygen must therefore be avoided and the tolerance to

oxygen carefully observed unless artificial ventilation is being performed as mentioned above In practice oxygen is either given intermittently at a flow rate of 6 l/min or continuously by mask at a flow rate not exceeding 2 l/min This may be increased as clinical improvement sets in and is continued until cyanosis has been abolished Additional treatment for heart failure may be required

DISEASES OF THE PLEURA

Pleurisy

The term pleurisy simply means inflammation of the pleura In its simplest form there is hyperaemia and oedema of the pleural surfaces with some fibrinous exudate only (dry pleurisy) In other cases the inflammation is accompanied by an outpouring of fluid (pleurisy with effusion) and in some the fluid is purulent (purulent pleurisy empyema) Although these are separable clinical entities it must be appreciated that one may progress to the other and all three may be encountered in succession in one patient In addition a pleural effusion can occur as a transudate in the absence of inflammation

Dry Pleurisy

Aetiology Sometimes the aetiology is obscure but in most cases dry pleurisy is infective in origin and it may complicate many pulmonary diseases Thus it may accompany bronchitis or pneumonia lung absces bronchiectasis tuberculosis or bronchial carcinoma Infection may also reach the pleura from below the diaphragm particularly in subphrenic abscess or from the chest wall by direct spread or penetrating injury A primary infective form with an epidemic tendency is known as epidemic dry pleurisy or Bornholm disease and is probably due to a virus Non infective pleurisy *occurs in association with closed injuries of the* chest pulmonary infarction and neoplastic infiltration

Clinical Picture A sharp stabbing pain aggravated by deep breathing or coughing is the characteristic feature Its intensity varies from a slight stab at the height of inspiration to acute agony even on quiet breathing It is felt over the inflamed area in most cases but when the diaphragmatic pleura is involved pain is frequently referred to the shoulder or upper abdomen

The diagnostic sign is pleural friction heard in most cases over the site of maximum pain It is a coarse grating or creaking sound varying with the depth of respiration and may be palpable as pleural fremitus Chest movement is suppressed because of the pain breathing is rapid and shallow and the breath sounds are consequently diminished On the left side inflammation of the pleura in contact with the pericardium may give rise to pleuro pericardial friction the pleural element ceasing when the breath is held and the pericardial element continuing synchronously with the heart beat. Pleurisy is usually accompanied by a dry cough fever and symptoms of general illness and often by other signs in the lungs due to the underlying disease

There are no characteristic radiographic signs of pleurisy *per se* Slight pleural thickening may be *seen and on radioscopy the diaphragm may be ill* defined and restricted in its movement on the affected side

Differential Diagnosis If pleural friction is detected the diagnosis of pleurisy is established but its aetiology must be sought A coarse rhonchus is distinguished from a pleural rub since it is modified or dispersed by coughing muscular sounds (susurrus) are clearly related to muscular action When no rub is audible difficulty may arise over intercostal muscle sprains and fractured ribs which are sometimes the result of coughing Local tenderness the absence of constitutional symptoms and radiography will help in the differentiation A slipping costal cartilage is detected by *its* mobility the recurrent nature of the pain and its close relation to a particular movement *e g* bending down The pre-eruptive stage of herpes zoster is accompanied by severe pain but this is constant and unrelated to respiration In basal pleurisy with pain referred *to the upper abdomen the associated hyper*aesthesia and muscular rigidity may closely resemble an acute abdominal emergency

Clinical Course The course is related closely to that of the underlying disease If no effusion follows dry pleurisy subsides in a few days but a pleural rub may remain audible for a considerably longer period

Treatment The causal disease will require appropriate treatment but whatever the aetiology symptomatic treatment is often required for the relief of pain Local heat by means of a hot water bottle or electric pad relieves pain considerably and analgesics are given according to its severity Tab Codein Co (B P C) two 4 hourly will often suffice but pethidine 50–100 mg or morphine 10–15 mg (⅙–¼ gr) may be necessary for the first day or two Frequent useless cough should be suppressed with an effective linctus such as Linct Methadone 4 ml

(1 dr) or pill Codeín Phosph 30–60 mg (½–1 gr) Strapping the affected side of the chest in expiration is sometimes employed but has no particular advantage over the above measures and interferes with clinical examination Persistent severe pain as may be due to *neoplastic infiltration of the pleura* and chest wall may be relieved by blocking the intercostal nerves temporarily with procaine or permanently with alcohol

Epidemic Dry Pleurisy (Bornholm Disease Epidemic Myalgia)

An acute benign febrile illness the main clinical feature of which is acute pain around the lower chest or upper abdomen A pleural rub appears in about a third of the cases but it is undecided *whether the site of inflammation is primarily the diaphragm chest wall muscles or the pleura It is* almost certainly due to infection by one or other of the Coxsackie group of viruses as these organisms can be isolated from the stools and neutralizing antibodies are detectable in the serum in a proportion of patients *Sporadic cases are difficult* to diagnose but localized epidemics are not infrequent The pain is severe spasmodic and pleural in type but sometimes resembles that of renal colic or acute appendicitis Fever and severe headache *are usually present and occasionally vomiting* Recovery is the rule within 10–14 days but relapses are not infrequent either at short intervals or after a few months Complications include orchitis parotitis and lymphocytic meningitis

Pleurisy with Effusion

A non purulent exudate in the pleural space may *accompany inflammation of the pleura in a variety* of conditions A frequent and important cause is tuberculosis but an effusion may complicate many forms of pneumonia pulmonary infarction neoplasms and subdiaphragmatic infection Gen*eralized oedema from cardiac or renal disease may* also be accompanied by transudation of fluid into the pleura The physical signs in the chest are the same whatever the aetiology and differential diag*nosis rests upon other clinical features and examina*tion of the fluid

Tuberculous Pleural Effusion

A pleural effusion may develop at any stage in a *patient with active pulmonary tuberculosis but most frequently* it appears within 3–7 months of a primary infection in young adults It is often the first manifestation of tuberculosis in such patients the primary infection having passed unnoticed In the light of modern knowledge terms like idio*pathic* and benign should no longer be applied *to pleural effusions developing in young adults* even when a tuberculous aetiology cannot be proved The great majority are tuberculous and the title pleural effusion (presumably tuberculous) is preferable as indicating its potential dangers and the need for *careful follow up*

Clinical Picture Vague symptoms of ill health may precede the onset which is usually with pleural pain dry cough and fever The pain lessens as fluid accumulates but general malaise cough and fever *persist and dyspnoea gradually increases*

The physical signs in the chest depend upon the size of the effusion which gravitates to the base If it is small there will be a limited area of stony dullness at one base absent or weak breath sounds *and impaired movement A pleural rub and aegophony may be detected at the upper margin of dull*ness and sometimes the breath sounds are bronchial. With larger effusions these signs are more extensive and the mediastinum is displaced to the opposite side *(see p 312) Pulsus paradoxus is occasionally* observed with a massive pleural effusion

Radiography shows a basal opacity its upper border rising towards the axilla and mediastinal displacement The E S R is considerably raised *the blood count is usually normal but may show a relative lymphocytosis* The tuberculin skin test is positive and often strongly so

Diagnostic aspiration is advisable in all cases not only to confirm the presence of fluid *but to enable its character to be observed* and the aetiology to be established Needle biopsy of the parietal pleura can be performed at the same time with an Abram s needle and yields early positive histological confirmation of the diagnosis *in about 80 per cent of cases The paracentesis is performed* under local analgesia in the mid axillary line or over the area of dullness behind and at least 100 ml should be removed for examination The fluid is clear or very slightly turbid yellow *and forms a clot on standing It has the features* of an exudate *i e* S G of 1·015 or more and protein content of more than 3 per cent The cells are mainly lymphocytes *Exceptionally* in the early stages *polymorphs or eosinophils may predominate and* again rarely the fluid may be bloodstained Organisms are seldom found in the fluid on direct examination and ordinary cultures are sterile Selective media for the growth of *tubercle bacilli should* always be inoculated and incubated for at least 12 weeks before accepting a negative result Sputum if it is present or gastric contents should also be examined for *acid fast bacilli* in the same way *Expert laboratory examina*tion will produce positive evidence of tuberculosis in approximately 80 per cent of cases

Differential Diagnosis Extensive intrapulmonary lesions affecting the lower lobes may simulate a pleural effusion but in general the physical signs are sufficiently distinctive Pneumonia lobar atelectasis and malignant neoplasms are accompanied by cough and sputum large benign tumours and cysts are usually distinguished on their radiographic appearances Difficulty may arise in cases of diaphragmatic hernia and conditions associated with considerable elevation of the hemidiaphragm Radioscopy and barium studies often provide useful information but when doubt exists an exploratory puncture should be performed The presence of fluid having been confirmed the differential diagnosis then includes the other causes of pleural effusion dealt with below

Course and Complications The outlook is generally favourable with modern treatment The fluid usually absorbs within 6 weeks but the rate of absorption varies considerably from 3 or 4 weeks to as many months Pain subsides in a few days the fever and constitutional symptoms in a week or two Occasionally and especially if anti tuberculous drugs have not been given disseminated miliary tuberculosis develops Tuberculous empyema is uncommon except where the effusion is complicating progressive pulmonary tuberculosis Eventual absorption of the effusion with some pleural symphysis is the rule Some degree of pleural thickening may remain and at times this is extreme with considerable restriction and unilateral deformity of the chest In such cases the pleura may ultimately show calcification The most important sequel is active pulmonary tuberculosis in approximately 25 per cent of cases This figure refers to cases not treated by anti tuberculous drugs It is probable that with chemotherapy the incidence will be very much less

Treatment. General treatment is essentially the same as for patients with active pulmonary tuberculosis (*see* p 353) The initial period should be spent in hospital where full investigation can be made and nursing facilities are available Anti tuberculous drugs should be given as for pulmonary disease and should continue for at least a year Bed rest is advisable until the temperature has been normal for about a month and there are such signs of improvement as normal E S R and gain in weight In the average case this takes 2–3 months and a graduated programme of increasing activity is then instituted with regular checks by clinical radiographic and laboratory tests

After diagnostic aspiration small or moderate effusions can be left alone provided they show early progressive absorption and most of them do Large effusions may require aspiration to relieve dyspnoea Repeated aspiration of 1–2 pints may be necessary every few days but it is unwise to exceed 2 pints as there is a risk of pulmonary oedema Air replacement of the effusion is not recommended Delay in absorption of large effusions beyond 4–6 weeks leads to considerable pleural thickening and loss of lung function Such effusions therefore should be aspirated and often after the first aspiration absorption will proceed more rapidly Long term results of treatment of all cases by early aspiration anti tuberculous drugs systemically and streptomycin intrapleurally at each aspiration are not yet available but the early results are very good with regard to the rapidity of absorption and prevention of pleural fibrosis

Subsequent Treatment The period of graduated convalescence under medical supervision will take approximately another 3 months to the stage of being up all day and this period is ideally spent in a sanatorium Return to work at first part time is then usually possible with the gradual resumption of the normal activities of a quiet life Regular observation by chest radiographs is essential and should be repeated at least 3 monthly for 2 years and then 6 monthly for at least another 3 years This is the only means of detecting early those destined to develop pulmonary disease It seems probable that with long term chemotherapy this risk will be considerably reduced and that a more rapid return to a normal existence may become possible but at present it is still wise to err on the cautious side

Other Types of Pleural Effusion

Pleural Effusion with Pneumonia

Exudation of serous fluid into the pleura may accompany most forms of pneumonia particularly the bacterial varieties This complication is more common since effective antibiotics were introduced and some at least represent abortive empyemas The effusion is seldom large it contains polymorphs and sometimes bacteria and if inadequately treated may progress to an empyema The associated symptoms and signs of pneumonia and the laboratory examination of fluid usually serve to distinguish this type of effusion from the tuberculous variety

For all but the small effusions aspiration repeated if necessary is advisable to hasten recovery and to forestall the development of an empyema After each aspiration 500 000 units of crystalline penicillin G may be instilled into the pleural space and the routine chemotherapy for pneumonia should continue until it is evident that the effusion

has not re accumulated Should the fluid persist for more than 10–14 days the diagnosis should be re considered having particular regard to a tuber culous or underlying neoplastic aetiology

Pleural Effusions with Neoplasms

Pleural effusion occasionally accompanies benign tumours in the thorax but is more common with malignant growths A primary bronchial carcinoma is the commonest cause but secondary metastases from primary cancers in the breast stomach kid neys and ovaries are also frequent The fluid accumulates rapidly and is frequently bloodstained Malignant cells may be detected in the fluid In vestigation will include a full clinical examination and radiography and often bronchoscopy If un certainty remains thoracoscopy after pleural aspiration and possibly pleural biopsy will usually clinch the diagnosis The rare condition of Meig s syndrome consists of pleural effusion and ascites in association with a benign fibroma of the ovary The effusions absorb when the ovarian tumour is removed However in most patients who present with a pelvic mass peritoneal and pleural effusions the pelvic tumour proves to be malignant Malig nant effusions are incurable but temporary benefit is sometimes afforded by radiotherapy intrapleural radioactive gold ^{198}Au or hormone therapy where the primary site is the breast or prostate

Pleural Transudates (*Hydrothorax*)

The generalized oedema of cardiac failure renal disease or deficiency states may be accompanied by pleural effusion which may be bilateral The fluid is usually clear and yellow with a specific gravity of less than 1 015 a protein content of less than 3 per cent and it contains few cells Treatment is that of the underlying cause but aspiration may be needed to relieve respiratory distress

Chylous Pleural Effusion

A true chylous effusion (chylothorax) results from injury to the thoracic duct or other large lymph vessel or from lymphatic obstruction by malignant disease or filariasis The fluid has a milky appearance and contains free fat globules demon strable by staining with Sudan III Surgical repair of the thoracic duct is often impracticable Aspira tion should be performed only to relieve dyspnoea as the rapid loss of chyle leads to severe malnutri tion Long standing effusions from any cause may assume a milky appearance to the naked eye (pseudochylous) due to various suspended particles other than fat

Other Causes of Pleural Effusion

There remains a number of other conditions which may give rise to pleural effusion *Pulmonary infarction* is not uncommonly followed by a hae morrhagic effusion of small or moderate extent which seldom requires aspiration When it is associated with chronic left heart failure however the fluid may re accumulate and require aspiration until pulmonary congestion is relieved by treatment of the heart condition Infection below the dia phragm particularly subphrenic or liver abscesses may produce a basal pleurisy and some pleural exudation This may progress to an empyema but usually absorbs without incident if the primary lesion is recognized and treated Rheumatic fever in its acute form may cause pleurisy and effusion and the latter is also an occasional feature of some of the more chronic collagen diseases *e g* systemic lupus erythematosus and long standing rheumatoid arthritis

Haemothorax

Frank haemorrhage into the pleura as distinct from a bloodstained effusion is usually the result of chest injury Penetrating wounds and crush or blast injuries are common causes and it may com plicate surgical operations on the thorax A spon taneous variety due to rupture of pleural adhesions occurs sometimes in previously healthy individu als or in those suffering from pulmonary tubercu losis Occasionally rupture of an aortic aneurysm is the immediate cause

Pathology Blood in the pleural space clots promptly and the clot is then broken up by the cardiac and respiratory movements fibrin clots being deposited on the pleura or collecting at the bottom of the pleural space The heavily blood stained fluid which remains cannot clot having lost its fibrinogen but its irritating property leads to pleural exudation during the next few days The fibrinogen concentration therefore rises once more to reach a maximum in 7 days and secondary clot ting can then take place This secondary clotting can be avoided by early aspiration If the blood is not removed extensive organization of the clot will follow with severe limitation of pulmonary function

Clinical Picture In traumatic cases the clinical features will include those of the associated injuries The intrapleural bleeding may be slow over a period of hours or sudden and massive In the latter event the picture is that of haemorrhagic shock A smaller

haemorrhage gives rise to stabbing chest pain dys pnoea tachycardia and some degree of fever The signs in the chest are those of a pleural effusion or hydropneumothorax the extent varying with the size of the haemorrhage Upper abdominal rigidity is common and the clinical picture may resemble an acute abdominal emergency

Treatment Cases of massive or continuing hae morrhage require urgent transfusion and thoraco tomy In less severe cases the bleeding stops spontaneously and aspiration should begin as soon as shock has been relieved The object is to keep the pleural space as dry as possible and to prevent secondary clotting Intrapleural fibrinolytic enzymes *e g* streptokinase streptodornase are sometimes useful in liquifying the fibrin clots and aiding more complete aspiration Penicillin should be given systemically and intrapleurally to mini mise the risk of secondary infection and empyema Where aspiration fails or in neglected cases thoracotomy is advisable in order that pleural toilet and decortication can be effectively per formed to minimize the risks of infection loss of lung function and chest deformity

Empyema

Empyema Thoracis

Definition A collection of pus within the pleural space due to its invasion by pyogenic bacteria

Aetiology In most cases the pleura is involved by spread of infection from within the lung Thus an empyema may complicate the various forms of pneumonia or pulmonary suppuration of any kind Infection may also be introduced from outside by penetrating chest wounds surgical procedures or perforation of the oesophagus Less commonly the pleura is infected by direct spread from below the diaphragm

Classification and Pathology Empyemas may be classified according to their site *e g* basal lateral interlobar etc but more satisfactorily according to the causal organism *e g* pneumococcal strepto coccal staphylococcal tuberculous mixed infection etc

The first stage is one of acute pleurisy with fluid exudation Untreated the fluid gradually becomes more turbid until it consists of obvious pus the pleural surfaces adhere to localize the pus into a mature pleural abscess the walls of which are lined by a deposit of fibrin

Clinical Picture The development of an empyema as a complication of pneumonia under treatment is often insidious and the symptoms and signs merge with those of the pulmonary infection The possibility should always be considered when the response to specific treatment is delayed or when fever returns after having settled for a few days Toxaemia increases with sweating tachy cardia anorexia loss of weight pallor and usually a persistent leucocytosis in the blood Pleural pain is variable and dyspnoea is a feature when the empyema is large A more abrupt onset character izes the empyema resulting from gross soiling of the pleural space by rupture of a lung abscess or tuberculous cavity the patient being gravely ill within a few hours In most cases signs of pleural effusion (*see* p 312) can be elicited the distinction resting upon other clinical features and examination of the fluid In children the typical signs are often absent and in adults an empyema may be undetect able clinically by virtue of its small size or in accessible position

Diagnosis Final diagnosis rests upon exploratory needling and the withdrawal of pus Radiography in postero anterior and lateral planes will confirm the presence of an effusion and indicate the best site for puncture Cultures of the pus should always be made in order to identify the infecting organism and to guide treatment

Course and Complications Empyema is a serious condition especially in infants With skilled manage ment however most patients recover If the condi tion is unrecognized the pus may track through the chest wall to point on the surface (empyema necessitans ') alternatively it may rupture into the lung a large quantity of pus being suddenly ex pectorated Exceptionally this may effect a natural cure but more commonly a bronchopleural fistula remains leading to a chronic abscess cavity The most important complication however is *chronic empyema* which so often follows inadequate treat ment of the acute stage

Treatment The principles of treatment of acute non tuberculous empyema are (*a*) antibiotics in full dosage systemically and intrapleurally to combat the infection and (*b*) the evacuation of the pleural exudate and obliteration of the empyema space as soon as possible by re expansion of the lung Pending bacteriological examination of the fluid penicillin is given systemically 2 000 000 units daily in divided doses and 500 000–1 000 000 units intra pleurally at each aspiration Subsequent chemo therapy is determined by sensitivity tests Repeated aspiration daily or every other day is performed and as much fluid removed as possible In success- ful cases the fluid will be sterile it will gradually

has not re accumulated Should the fluid persist for more than 10–14 days the diagnosis should be re considered having particular regard to a tuberculous or underlying neoplastic aetiology

Pleural Effusions with Neoplasms

Pleural effusion occasionally accompanies benign tumours in the thorax but is more common with malignant growths A primary bronchial carcinoma is the commonest cause but secondary metastases from primary cancers in the breast stomach kidneys and ovaries are also frequent The fluid accumulates rapidly and is frequently bloodstained Malignant cells may be detected in the fluid Investigation will include a full clinical examination and radiography and often bronchoscopy If uncertainty remains thoracoscopy after pleural aspiration and possibly pleural biopsy will usually clinch the diagnosis The rare condition of Meig s syndrome consists of pleural effusion and ascites in association with a benign fibroma of the ovary The effusions absorb when the ovarian tumour is removed However in most patients who present with a pelvic mass peritoneal and pleural effusions the pelvic tumour proves to be malignant Malignant effusions are incurable but temporary benefit is sometimes afforded by radiotherapy intrapleural radioactive gold ^{198}Au or hormone therapy where the primary site is the breast or prostate

Pleural Transudates (Hydrothorax)

The generalized oedema of cardiac failure renal disease or deficiency states may be accompanied by pleural effusion which may be bilateral The fluid is usually clear and yellow with a specific gravity of less than 1 015 a protein content of less than 3 per cent and it contains few cells Treatment is that of the underlying cause but aspiration may be needed to relieve respiratory distress.

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A true chylous effusion (chylothorax) results from injury to the thoracic duct or other large lymph vessel or from lymphatic obstruction by malignant disease or filariasis The fluid has a milky appearance and contains free fat globules demonstrable by staining with Sudan III Surgical repair of the thoracic duct is often impracticable Aspiration should be performed only to relieve dyspnoea as the rapid loss of chyle leads to severe malnutrition Long standing effusions from any cause may assume a milky appearance to the naked eye (pseudochylous) due to various suspended particles other than fat

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Pneumothorax

Any breach of the pleural surfaces which permits communication of the potential pleural space with the atmosphere will allow air to enter the pleural sac by virtue of the subatmospheric pressure therein Thus a pneumothorax may follow penetrating wounds of the chest including the controlled in duction of an artificial pneumothorax by needle puncture The visceral pleura may be ruptured by closed injuries and fractured ribs and in a variety of pulmonary diseases both inflammatory and non inflammatory Occasional causes are perforation of the oesophagus and the transfer of air from the peritoneum to the pleura through defects in the diaphragm

Spontaneous Pneumothorax

Definition The sudden escape of air into the pleural space due to rupture of the visceral pleura

Aetiology In the majority of cases spontaneous pneumothorax arises from rupture of a small sub pleural air cyst or bulla The bulla itself derives from distended lung alveoli probably as a conse quence of check valve bronchiolar obstruction caused by the healing of a previous inflammatory lesion (penumothorax simplex) In some cases however the site of the pleural leak cannot be identified on the surface of the lung A possible ex planation of this type is that the primary event may be alveolar rupture in the substance of the lung and that the interstitial air tracks along the peri vascular and peribronchial spaces to the medias tinum and eventually ruptures through the mediastinal pleura

Apart from the common type spontaneous pneu mothorax may complicate many pulmonary dis eases Rupture of a subpleural tuberculous focus is perhaps the second most common cause while a minority occur with such conditions as generalized hypertrophic emphysema lung abscess (especially staphylococcal) bronchial carcinoma and cystic disease of the lungs

Men are more frequently affected than women particularly in early adult life but no age is immune

Types of Spontaneous Pneumothorax The nature of the pleural tear determines the type of pneumo thorax Commonly it is a small hole which seals over as the lung collapses and leakage of air is arrested while the intrapleural pressure is still sub atmospheric (simple or closed pneumothorax) A large pleural tear may not close spontaneously and air continues to enter the pleura until the mean pressure is atmospheric The lung remains collapsed air entering and leaving the pleural space in in spiration and expiration via the fistula Such cases are more commonly associated with tuberculous or other pulmonary disease and infection of the pleura is likely to follow (pyopneumothorax) In a third variety a flap of torn pleura or lung may close the breach in expiration but open it in inspiration and particularly during coughing This permits air to enter the space under positive pressure but its egress is prevented and an acute emergency may arise from severe displacement of the mediastinum and respiratory embarrassment (tension pneumothorax) In some cases although recovery seems to be com plete the underlying pleural defect remains and the condition recurs at intervals of a few months or years In a few also the pleura remains uninfected although a bronchopleural fistula exists and the pneumothorax becomes chronic

Clinical Picture The severity of the symptoms is variable but typically the onset is abrupt with sharp pain in the chest followed by dyspnoea or a sense of constriction The pain is no guide to the size of the pneumothorax but the degree of dyspnoea is usually in direct proportion The condition occurs as commonly at rest as during physical effort In some patients the symptoms are so mild that medical advice is not sought In others the on set is more gradual with the symptoms increasing over several days whereas in those with a tension pneumothorax the patient may quickly become acutely distressed and shocked Physical signs in the chest may be absent with a localized or shallow pneumothorax On rare occasions a shallow pneu mothorax especially if on the left side is accom panied by a clicking sound synchronous with car diac systole and changing with the position of the patient It may be so loud as to be audible to the patient or to the examiner without a stethoscope In the average case however there is diminished movement hyperresonance loss of the normal areas of dullness weak or absent breath sounds and no added sounds Mediastinal displacement to the opposite side may be apparent and in the tension type the affected side of the chest may appear distended and the coin sound may be de tectable (*see* pp 311 and 312) Cyanosis tachy cardia and respiratory distress will also be evident

Radiological examination shows the sharp linear margin of the partially-deflated lung with a trans lucent area devoid of lung markings between it and the chest wall In doubtful cases a radiograph should be taken in full expiration Occasionally sur face blebs or causal intrapulmonary lesions may be visible

Diagnosis and Differential Diagnosis In many

assume a serous quality and steadily diminish in amount In other cases although lessening in amount and sterile on culture it may continue to thicken and become more purulent until when a specimen is allowed to stand in a test tube seven eighths of its volume is thick pus and the upper one eighth is serous fluid At this stage the instillation of streptokinase streptodornase is worth trying as it may produce enough liquefaction to allow continued and complete aspiration and final cure If however the aspirate remains purulent or is too thick to be readily removed by needle puncture this method should be abandoned in favour of rib resection and drainage or excision of the empyema It must be emphasized that open drainage is contraindicated in the formative stage of suppurative pleurisy before the empyema is walled off from the general pleural cavity The optimum site for drainage is determined by radiography after instillation of iodized oil into the cavity Rib resection is advisable for complete evacuation of fibrin clots and debris and gentle suction may be used in the post operative period Breathing exercises and trunk exercises are begun immediately after operation and practised at least 2 hourly to encourage re expansion of the lung The general health improves rapidly after evacuation of the pus and the patient is encouraged to get up within a few days of the operation A high protein diet and iron are recommended during convalescence to hasten full recovery of nutrition and the secondary anaemia The drainage tube should not be removed until the cavity has completely closed and only the tube track remains Periodic injection of iodized oil into the tube and subsequent radiography will enable this time to be decided as it varies from a few weeks to several months

Chronic Empyema

Chronic empyema usually arises as a result of inadequate treatment of an acute empyema If medical treatment has been persisted in too long or if the empyema has passed unrecognized its walls become progressively more thickened and rigid and may prevent re expansion of the lung when drainage is eventually performed In a large empyema also loculation may take place Faulty surgical management is another causal factor as when the drainage tube is placed too high or when it is removed too early before obliteration of the space Other causes of chronicity are the presence of foreign bodies in the pleura a bronchopleural fistula and an underlying new growth Sometimes the nature of the infecting organism is chronic and persistent e g tuberculosis actinomycosis

Patients with chronic empyema suffer from general ill health Loss of weight and strength anaemia and episodes of exacerbation of chest pain fever cough and sputum are common Clubbing of the fingers develops and occasionally amyloidosis Considerable deformity of the chest may arise as nature endeavours to close the abnormal space by sinking in of the chest wall spinal curvature mediastinal displacement and elevation of the diaphragm Full investigation is necessary to determine the cause Repeated cultures of the pus radiographs including pleurograms and bronchography bronchoscopy and pleural biopsy may all be required to ascertain the reason for chronicity The treatment is to remedy the cause when possible In most cases it is a surgical problem and varies from simple re drainage in the correct site to total excision of the empyema sac with the whole or part of a diseased lung

Tuberculous Empyema

Tuberculous empyema is now a comparatively rare complication of pulmonary tuberculosis Most cases arose in patients undergoing treatment by artificial pneumothorax either spontaneously or following adhesion section (*see* Plate 16 9) With the decline in this form of treatment and the better understanding of the type of cases suitable for it the incidence of tuberculous empyema has fallen considerably Nevertheless it occasionally complicates pulmonary tuberculosis or develops from a tuberculous pleural effusion It is always a serious condition with a high morbidity and mortality

Moderately acute symptoms of malaise fever and pleural pain are sometimes experienced but in most cases the onset is insidious with the accumulation of serous fluid in the pleura Tubercle bacilli may be grown from this fluid and there is usually active disease in the underlying lung Over the course of many weeks or months the fluid accumulates gradually becoming turbid and finally purulent Treatment is by repeated aspiration intra pleural streptomycin and anti tuberculous drugs systemically and is aimed at obliteration of the pleural space as soon as possible In long standing cases thickening of the visceral pleura prevents further re-expansion of the lung and the choice of treatment then lies between total excision of the empyema sac sometimes combined with pulmonary resection and a thoracoplasty Open drainage is contra indicated except with secondary infection and a bronchopleural fistula In such it may have to be undertaken as an urgent temporary measure to avoid the risk of drowning or bronchogenic dissemination

vised by tying a rubber finger cot or the finger of a rubber glove around the cannula and making a slit in the end

The initial treatment of spontaneous pneumothorax complicating tuberculosis is the same as that for the simple variety as regards adjustment of intrapleural pressure This type is commonly followed by a pleural effusion and tuberculous empyema Anti tuberculous drugs are therefore given systemically and intrapleurally and early obliteration of the space is encouraged if necessary by continuous suction It is seldom justified to maintain the pneumothorax as a therapeutic procedure

A simple pneumothorax which recurs more than once is likely to continue to do so at intervals In such cases and in all chronic pneumothoraces full investigation of the cause should be made the most useful examination being thoracoscopy This may reveal a large bulla or cyst which can be dealt with only by surgical excision Where no obvious cause is found or where the pleural flaws are numerous and widespread pleural symphysis may be secured by inducing an aseptic pleurisy by means of chemical irritants applied direct to the visceral pleura at thoracoscopy or injected through the chest wall under local analgesia Many substances have been used for this purpose the most reliable being 1 per cent iodine in talc powder a 25 per cent suspension of kaolin in distilled water or 10 per cent silver nitrate For a detailed consideration of these measures more specialized textbooks must be consulted

Neoplasms of the Pleura

New growths of the pleura are very rare A pedunculated fibroma is the commonest benign tumour but it is more probable that it arises in the subpleural lung tissue It is usually discovered on routine radiography occasionally reaches large proportions and in a percentage of cases causes a generalized arthropathy which is dramatically relieved by its removal Pseudo fibromas arise from organization of a fibrin body formed during a pleural effusion

Of the malignant tumours the mesothelioma presents with a rapid and recurring pleural effusion and diagnosis can be made only by thoracoscopy and pleural biopsy Most pleural endotheliomas are now regarded as peripheral bronchial carcinomas invading the subpleural lymphatics

Pulmonary Cysts

Cysts of the lungs may contain air fluid or both but too little is known of their origin to permit of an accurate aetiological classification Some are undoubtedly congenital but the majority are acquired Many are symptomless and are discovered only on routine radiographs Symptoms if any result from progressive enlargement from secondary infection or from rupture of the cyst

Air containing Cysts

Distension of alveolar spaces often with disruption of interalveolar septa is a common process by which pulmonary cysts arise The mechanism is the same as that operating in emphysema and the cysts are usually multiple Not infrequently such cysts are found in the absence of generalized obstructive emphysema presumably arising in consequence of a valvular communication with the bronchial tree resulting from preceding local pulmonary disease Progressive enlargement sometimes leads to severe respiratory distress necessitating surgical excision of the cyst This type is seen also in infants when its fundamental cause is unknown

Similar air containing spaces in the lungs are occasionally the sequel to pulmonary infections Lung abscess particularly the staphylococcal variety and occasionally a tuberculous cavity may heal in so far as the infection is overcome but a thin walled cyst remains and is maintained or even enlarges because of a persistent check valve bronchial communication

Bronchogenic Cysts (Fore-gut Cysts)

These are developmental in origin and usually single It is probable that they arise from the isolation of a primitive lung bud in foetal life The walls contain respiratory epithelium and variable amounts of all the bronchial elements muscle cartilage mucous glands fibrous and elastic tissue arranged haphazardly If no bronchial communication exists such cysts are filled with fluid and cast a homogeneous shadow on the radiograph Often however there is a bronchial fistula so that the cyst also contains air and a fluid level Under these circumstances secondary infection tends to supervene sooner or later The clinical features are then similar to those of a lung abscess and excision of the cyst or lung segment containing the cyst is necessary

More complete separation of a primitive lung bud occasionally results in a dissociated segment of

cases the history and clinical examination are distinctive but radiography is advisable for confirmation and as part of the investigation of the aetiology Similar symptoms may be given by pulmonary embolism coronary thrombosis pulmonary atelectasis pericarditis and acute pleurisy The chest signs may be indistinguishable from unilateral obstructive emphysema or a large air cyst The combination of clinical and radiological examination resolves these difficulties

Course and Complications In pneumothorax simplex the prognosis is good The air is absorbed over a period of 3–6 weeks and the lung re expands fully A trace of fluid is often seen in the costo phrenic angle but this does not increase and the patient remains afebrile throughout Haemorrhage may occur into the pleura at the onset (haemopneumothorax) but pleural infection is very unusual Recurrence is not uncommon and in a few patients the condition becomes chronic The open type with a bronchopleural fistula is commonly followed by pleural infection Spontaneous pneumothorax occurring as a result of a subpleural tuberculous focus is accompanied by fever and a raised E S R and is nearly always followed by a progressive effusion which may become a tuberculous empyema In cases secondary to other forms of pulmonary infection also the pleura is commonly infected and a pyopneumothorax develops

Treatment Simple non tuberculous spontaneous pneumothorax requires no active treatment as a rule Air should not be removed from the pleura unless breathing is distressed Cough should be discouraged by abstaining from tobacco and by a sedative linctus if necessary The patient should rest until serial radiographs show that re expansion has begun and he may then be allowed up gradually Exertion is avoided until re expansion is complete and severe effort for 2–3 months

A tension pneumothorax may prove rapidly fatal unless air is promptly withdrawn from the pleural space Oxygen should be administered during the necessary procedure Under local anaesthesia a needle attached to an artificial pneumothorax apparatus is inserted through an intercostal space usually the fifth in the mid axillary line or the second in the mid clavicular line The pressure which will be positive is noted and sufficient air is aspirated to reduce it to zero Relief is usually dramatic More air should not be removed unless breathing remains difficult as reduction of the pressure to sub atmospheric may encourage a further escape of air from the lung and delay healing of the surface tear The needle is held in place for some minutes while the intrapleural pressure is observed with a manometer If it remains at zero the needle can be safely withdrawn but the apparatus should remain at hand in case the procedure has to be repeated On the other hand if the pressure gradually rises once more a valvular mechanism is still operating and a continuous form of decompression is required The needle is replaced by a small flanged cannula (Foster Carter needle) or a self retaining rubber catheter (Foley type) which is connected by a rubber tube to an underwater seal placed on the floor beside the bed (Fig 16 3) The cannula may be removed 24 hr after air has ceased to be blown off In an emergency a simple valve may be impro-

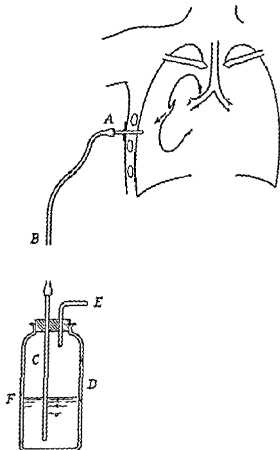


Fig 16 3 Under water Seal

The cannula *A* or rubber catheter is inserted a minimum distance through the parietal pleura Rubber tubing *B* connects this to glass tube *C* the lower end of which is below the level of water in bottle *D* Air escapes through outlet valve *E* whenever a positive pressure is reached in the pleura When the pleural leak seals off and the air begins to absorb the negative pressure is shown by the water level rising up the tube *C* and its fluctuation during respiration The level *F* should be at least 2 ft below the level of the cannula and the bottle must not be lifted without firmly clipping the tube *B* otherwise water will be sucked into the thorax

rarity They are usually peripheral but sometimes endobronchial. In the former circumstances they produce no symptoms and are discovered on routine radiographs and in the latter the symptoms are referable to bronchial obstruction and infection. The chest radiograph usually shows a circumscribed peripheral shadow sometimes with calcification within it. It may be impossible to distinguish from a primary or secondary malignant neoplasm and in such circumstances resection is advisable Calcification in the tumour virtually excludes malignancy and such cases may be observed to remain stationary for many years

Vascular Tumours

Localized haemangiomas are occasionally discovered in the lungs and mediastinum and are sometimes multiple An important variety is the arterio-venous aneurysm since it may produce severe haemoptysis. The arterio-venous shunt in the lungs is accompanied by cyanosis secondary polycythaemia and clubbing of the fingers and a localized machinery murmur may be audible over the tumour The characteristic radiological appearance is of a lobulated soft shadow connected to the hilum by a leash of abnormally wide blood vessels. Angiography confirms the diagnosis but is often unnecessary Treatment is by segmental resection and ligation of vessels.

Other benign tumours are extremely rare but include lipoma fibroma, leiomyoma, and neurofibroma They have no specific features to enable a diagnosis to be made before they are removed and examined histologically

Primary Bronchial Carcinoma (Syn. Cancer of the Lung)

Definition. A malignant neoplasm arising from bronchial epithelium or glandular components of the bronchial mucosa

Incidence. Bronchial carcinoma is much the commonest intrathoracic neoplasm and has shown an alarming increase during the past 30 years. It attacks males more frequently than females in the ratio of 8 or 9 1 and in England is now the commonest visceral cancer in men It is uncommon before the age of 20 yr but not rare between 20 and 40 yr The highest incidence however is from 45 to 65 yr when it accounts for more than 10 per cent of all male deaths Only a small proportion of this increased incidence can be explained on the basis of improved diagnosis and the increased average age of the population. There is no doubt that the increase is real. The number of deaths has risen steadily from below a thousand per annum in the 1920 s to more than 19 000 in 1958

Aetiology The exact aetiology is unknown and it is unlikely that a single factor is responsible From the accumulation of a vast amount of statistical and experimental research certain clues emerge which point to various aetiological factors most of them inhaled potential carcinogens A high incidence of the disease has been reported among miners at Schneeberg in Bavaria The ore contains sulphides and arsenides of nickel and cobalt and is radioactive opinion remains divided as to the respective importance of the arsenic the nickel, and the radioactivity However arsenic has been further incriminated since an increased incidence of bronchial carcinoma is found in workers employed in the manufacture of arsenical sheep dips Of possible importance is the fact that it is present in small amounts in tobacco smoke Other occupational hazards which carry an increased risk of the disease are asbestosis and exposure to chromates and coal tar derivatives. The disease is more common in city dwellers than in country folk and atmospheric pollution by chimney smoke and the exhaust gases of petrol and diesel engines may be a factor causing this difference Evidence on this point, however is inconclusive although a known carcinogen, 3 4-benzpyrene is present in such smokes

Of much greater importance is the relationship which has been shown to exist between smoking and lung cancer This applies more to the squamous and undifferentiated types than to the adenocarcinoma. It is the heavy cigarette smoker more than 25 per day who is at greatest risk, and indulgence in the habit to this extent over a period of 20 years increases the chances of developing lung cancer fifty fold The incidence of the disease seems to be proportional to the amount smoked. Pipe smokers incur less risk and some protection is afforded by filter tips and cigarette holders. The factor in tobacco smoke which is responsible remains unknown. Carcinogenic substances detectable include 3 4-benzpyrene 1,2 benzanthracene and arsenic but the evidence is at present insufficient to incriminate any or all of these with certainty

Pathology Three main histological types are distinguishable The *oat-celled* or anaplastic carcinoma is a poorly-differentiated growth with little stroma It is the most malignant and metastasizes early to the mediastinal lymph nodes Bronchial carcinoma in young subjects is commonly of this type The *squamous carcinoma* shows varying degrees of differentiation, being composed of flattened epithelial cells sometimes with keratinization and cell nests It occurs peripherally or centrally often undergoes

cystic lung which derives its blood supply from systemic vessels usually the aorta Bronchial communication usually exists or is established as a result of suppuration, and the clinical picture is one of infected bronchiectasis often with severe haemoptysis

Cystic Bronchiectasis

Spherical dilatation of the terminal bronchioles in a segment or lobe of lung is referred to as saccular or cystic bronchiectasis The radiographic appearance has been likened to a bunch of grapes but when the spaces are infected multiple fluid levels can be seen In most cases the condition is acquired and develops as a sequel to pulmonary atelectasis In some instances, however the coincidence of congenital abnormalities in other organs together with a history devoid of any suggestion of previous pulmonary disease is presumptive evidence that the cystic area of lung may be developmental in origin Treatment is not required unless secondary infection supervenes when it is that of infected bronchiectasis

Honeycomb Lungs

This is a descriptive term applied to a group of conditions of varied aetiology in which there are numerous thin walled cysts uniformly distributed throughout the substance of both lungs The cysts seldom exceed 1 cm in diameter and may or may not be lined by epithelium In some cases the pulmonary cysts are the only abnormality and their aetiology is a matter for speculation Possibly some are congenital and others represent the end r k of a generalized interstitial inflammation Similar honeycomb lungs are however found in association with other diseases notably xanthomatosis tuberous sclerosis certain reticuloses and pituitary disorders The presenting pulmonary symptom is increasing dyspnoea and such patients are liable to recurrent spontaneous pneumothoraces and right heart failure

Hydatid Cyst

Man and sheep are the intermediate hosts for *Echinococcus granulosus* a small tape worm which infests dogs Ova which are ingested hatch out into embryos which enter the portal circulation Most are arrested in the liver but occasionally the systemic circulation is reached and any organ may be involved In the lung as elsewehere they grow slowly to produce spherical or lobulated fluid filled cysts which may reach the size of a grapefruit Apart from their size they are potentially dangerous as secondary infection is not uncommon Aids to diagnosis are provided by the blood count which shows an eosinophilia a complement fixation test and the Casoni skin test Resection is recommended if feasible great care being taken to avoid rupture of the cyst which may evoke a violent allergic reaction and subsequent metastatic cysts in the contaminated area

NEOPLASMS

Benign Neoplasms of the Lungs and Bronchi

Innocent tumours of the lungs and bronchi are relatively uncommon comprising about 2 per cent of all intrapulmonary new growths

Bronchial Adenoma

This is the commonest innocent tumour the usual site being one of the larger bronchi A polypoid intrabronchial tumour is the usual presentation but the main mass of the tumour may be extrabronchial as a result of local invasion. Malignant change with lymphatic metastases is only an occasional complication The rate of growth is slow so that symptoms may have been present for several years before diagnosis Women are more often affected than men and a frequent early symptom is haemoptysis repeated at intervals sometimes for years before other symptoms arise An unproductive cough is common sometimes with dyspnoea and unilateral wheezing Sooner or later however the intrabronchial portion becomes large enough to impair bronchial drainage and varying degrees of pulmonary atelecta is and secondary infection occur The clinical picture is then similar to that of bronchiectasis with chronic cough purulent sputum and recurrent attacks of pneumonia In the early stages before the onset of bronchial occlusion the adenoma is seldom recognizable on chest radiographs and bronchoscopy is essential for diagnosis The only satisfactory treatment is by local resection which may have to include the segment or lobe in cases with longstanding secondary infection

Hamartoma

This is a benign tumour containing any or all the tissues found in normal lung Cartilage is the main component but muscle fat and fibrous tissue are also found Although thought to arise from embryonic rests malignant change is an extreme

rarity They are usually peripheral but sometimes endobronchial In the former circumstances they produce no symptoms and are discovered on routine radiographs and in the latter the symptoms are referable to bronchial obstruction and infection The chest radiograph usually shows a circumscribed peripheral shadow sometimes with calcification within it. It may be impossible to distinguish from a primary or secondary malignant neoplasm and in such circumstances resection is advisable Calcification in the tumour virtually excludes malignancy and such cases may be observed to remain stationary for many years

Vascular Tumours

Localized haemangiomas are occasionally discovered in the lungs and mediastinum and are sometimes multiple An important variety is the arterio venous aneurysm since it may produce severe haemoptysis The arterio venous shunt in the lungs is accompanied by cyanosis secondary polycythaemia and clubbing of the fingers and a localized machinery murmur may be audible over the tumour The characteristic radiological appearance is of a lobulated soft shadow connected to the hilum by a leash of abnormally wide blood vessels Angiography confirms the diagnosis but is often unnecessary Treatment is by segmental resection and ligation of vessels

Other benign tumours are extremely rare but include lipoma fibroma leiomyoma and neurofibroma They have no specific features to enable a diagnosis to be made before they are removed and examined histologically

Primary Bronchial Carcinoma (Syn Cancer of the Lung)

Definition A malignant neoplasm arising from bronchial epithelium or glandular components of the bronchial mucosa

Incidence Bronchial carcinoma is much the commonest intrathoracic neoplasm and has shown an alarming increase during the past 30 years It attacks males more frequently than females in the ratio of 8 or 9 1 and in England is now the commonest visceral cancer in men It is uncommon before the age of 20 yr but not rare between 20 and 40 yr The highest incidence however is from 45 to 65 yr when it accounts for more than 10 per cent of all male deaths Only a small proportion of this increased incidence can be explained on the basis of improved diagnosis and the increased average age of the population There is no doubt that the increase is real The number of deaths has risen steadily from below a thousand per annum in the 1920 s to more than 19 000 in 1958

Aetiology The exact aetiology is unknown and it is unlikely that a single factor is responsible From the accumulation of a vast amount of statistical and experimental research certain clues emerge which point to various aetiological factors most of them inhaled potential carcinogens A high incidence of the disease has been reported among miners at Schneeberg in Bavaria The ore contains sulphides and arsenides of nickel and cobalt and is radioactive opinion remains divided as to the respective importance of the arsenic the nickel and the radioactivity However arsenic has been further incriminated since an increased incidence of bronchial carcinoma is found in workers employed in the manufacture of arsenical sheep dips Of possible importance is the fact that it is present in small amounts in tobacco smoke Other occupational hazards which carry an increased risk of the disease are asbestosis and exposure to chromates and coal tar derivatives The disease is more common in city dwellers than in country folk and atmospheric pollution by chimney smoke and the exhaust gases of petrol and diesel engines may be a factor causing this difference Evidence on this point however is inconclusive although a known carcinogen 3 4 benzpyrene is present in such smokes

Of much greater importance is the relationship which has been shown to exist between smoking and lung cancer This applies more to the squamous and undifferentiated types than to the adenocarcinoma It is the heavy cigarette smoker more than 25 per day who is at greatest risk and indulgence in the habit to this extent over a period of 20 years increases the chances of developing lung cancer fifty fold The incidence of the disease seems to be proportional to the amount smoked Pipe smokers incur less risk and some protection is afforded by filter tips and cigarette holders The factor in tobacco smoke which is responsible remains unknown Carcinogenic substances detectable include 3 4 benzpyrene 1 2 benzanthracene and arsenic but the evidence is at present insufficient to incriminate any or all of these with certainty

Pathology Three main histological types are distinguishable The *oat celled* or anaplastic carcinoma is a poorly-differentiated growth with little stroma It is the most malignant and metastasizes early to the mediastinal lymph nodes Bronchial carcinoma in young subjects is commonly of this type The *squamous carcinoma* shows varying degrees of differentiation being composed of flattened epithelial cells sometimes with keratinization and cell nests It occurs peripherally or centrally often undergoes

central necrosis and is somewhat less malignant than the anaplastic type The *columnar celled or adenocarcinoma* is the least common and consists of cuboidal or columnar cells with a tendency to an alveolar arrangement and a variable secretion of mucin

Macroscopically the tumours appear as solid greyish white masses sometimes with central necrosis Peripheral growths often invade the pleura and may be associated with a blood stained effusion Those occurring in the major bronchi present an ulcerated nodular surface and varying degrees of bronchial stenosis Sooner or later obstruction to segmental lobar or main bronchi becomes complete with distal atelectasis Secondary infection with suppuration and bronchiectasis is common and may spread to the pleura giving rise to an empyema Direct invasion of the mediastinum with involvement of pericardium, heart aorta vagus recurrent laryngeal and phrenic nerves or oesophagus may occur, in addition to the frequent deposits in the regional lymph nodes

All types of bronchial carcinoma may metastasize early by the lymphatics or blood stream Lymphatic spread involves the draining lymph nodes first with subsequent extension upwards to nodes in the supra clavicular fossae or downwards to reach those in the retro peritoneal area Retrograde lymphatic permeation throughout both lungs is occasionally seen (lymphangitis carcinomatosa) Haematogenous metastases are usually multiple and may be found in any organ the commonest sites being the brain liver bones adrenals and skin

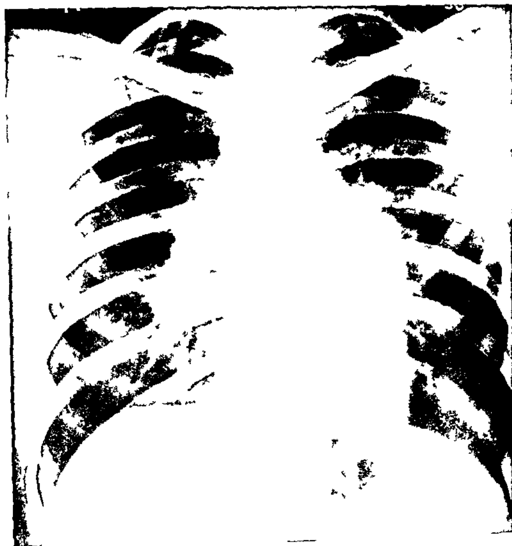
Clinical Picture There may be no symptoms early in the disease particularly if the neoplasm is peripherally situated Often by the time symptoms are present curative treatment is impossible Not infrequently the first evidence is in a site remote from the primary tumour and attributable to complications or metastases Hilar growths produce chest symptoms sooner or later and any patient over the age of forty who develops such symptoms however slight which persist for more than three weeks should be investigated as a carcinoma suspect As a rule the initial symptom is cough at first irritative and producing only a little mucoid sputum Haemoptysis a common symptom during the course of the disease is the first symptom in about 10 per cent of cases As the growth increases in size and encroaches on the bronchial lumen *obstructive emphysema* is occasionally produced but sooner or later partial or complete atelectasis of a segment lobe or whole lung occurs with retention of secretions and secondary infection The symptoms now become more marked Sputum increases and becomes purulent, often blood stained and sometimes offensive Attacks of fever are common the clinical picture suggesting a pneumonia which is slow to resolve A lung abscess or empyema may follow and be drained surgically without the underlying disease being realized until the persistent broncho pleural fistula arouses suspicion Dyspnoea is a common complaint when atelectasis has occurred but may be a severe symptom before bronchial obstruction is complete It seems to be due to fixation of the hilum by infiltrating growth so that its normal descent during inspiration is prevented and pulmonary expansion thereby diminished A persistent wheeze sometimes localized is not uncommon and stridor may be detectable Pleural pain is a late symptom except with a peripheral neoplasm but a large pleural effusion may be present when the patient is first seen

Apart from purely chest symptoms there are several well recognized clinical presentations some of them common others unusual Hoarseness from left vocal cord paralysis due to involvement of the left recurrent laryngeal nerve may be the first complaint A growth at the apex of the lung may declare itself with pain in the shoulder and arm from brachial plexus involvement and rib erosion there may also be an associated Horner s syndrome due to cervical sympathetic paralysis (Pancoast s tumour Superior Sulcus Tumour) A peculiar form of lung cancer is known as *alveolar cell carcinoma* or *pulmonary adenomatosis* The site of origin of this tumour is obscure but pathologically the alveoli are lined by mucus secreting columnar or cuboidal cells It often seems to have a multi-centric origin but an alternative view is that new foci arise by intrabronchial dissemination of malignant cells from the primary site The main symptoms are severe cough with a large quantity of frothy sputum which is often blood stained One or other of the complications listed below may be the first manifestation particularly important being the arthropathy and the central nervous manifestations

Physical examination of the chest may reveal no abnormal signs and the general condition and state of nutrition may be good As in the case of tuberculosis the absence of clinical signs does not exclude the disease and suggestive symptoms demand further investigation Encroachment on the bronchial lumen can sometimes be suspected from a localized wheeze From a consideration of the pathological changes in different cases it will be realized that physical signs of unilateral emphysema atelectasis consolidation bronchiectasis or pleural effusion may on occasions be found When pulmonary infection is established clubbing of the fingers is common and the general condition deteriorates



SILICOSIS



HILAR NODE ENLARGEMENT IN SARCOIDOSIS

PLATE 16 16

with lassitude anaemia irregular fever and progressive loss of weight Clinical examination must always be thorough and extend beyond the chest to detect metastases Careful palpation of the supraclavicular region for lymph nodes inspection of the cervical venous pressure palpation of the liver and a search for skin nodules are all essential as a positive finding in these respects means a hopeless prognosis

Radiography of the Chest Occasionally the chest radiograph is within normal limits the shadow of a small hilar growth being unobserved within that of the normal hilum In most cases however the radiograph is abnormal Commonly one or other hilar shadow appears prominent or there may be an obvious dense mass at the hilum (Plate 16 10) Atelectasis of a segment lobe or lung is commonly seen either as the sole abnormality or in association with a hilar opacity (Plate 16 11) The mediastinum may be widened and a chain of enlarged lymph nodes may be apparent alongside the trachea Peripheral tumours appear at first as small circumscribed opacities sometimes lobulated and when large may show cavitation the appearance suggesting a thick irregular walled lung abscess The ipsilateral hemidiaphragm may be raised due to phrenic paralysis a pleural effusion may be present, and there may be rib involvement either by direct invasion or metastatic deposit

Differential Diagnosis From a study of the protean clinical and radiographic manifestations of bronchial carcinoma it will be evident that the differential diagnosis includes a number of lung diseases too large to enumerate The various causes of bronchial obstruction and pulmonary suppuration pulmonary tuberculosis pleural effusion and empyema must all be considered as must also the various mediastinal tumours and adenopathies

Diagnostic Measures. Clinical appraisal should suggest the diagnosis as a possibility and the additional information provided by a plain radiograph will often render this a probability A normal radiograph does not exclude the diagnosis and in the face of suggestive symptoms further investigation is necessary final proof depending upon histological examination

Bronchoscopy In a high proportion of cases bronchoscopy provides positive evidence New growths in the main bronchi and their primary divisions are readily seen and a biopsy can be taken At the same time fixation of the main bronchi or distortion and widening of the carina provide evidence of inoperability Peripheral growths will not be visible but bronchial secretion aspirated from the segmental bronchus may contain malignant cells

Other Radiological Procedures Bronchography is sometimes of value in demonstrating bronchial obstruction beyond the field of vision of the bronchoscope Tomography angiography and a barium swallow also yield additional information on occasions but none of these measures provides proof of diagnosis

Malignant Cells in the Sputum The reliability of this test depends upon the experience of the pathologist. In expert hands malignant cells can be demonstrated in sputum or bronchial secretion in 60–70 per cent of cases with few false positives Its chief value is in the diagnosis of peripheral tumours which are beyond the reach of biopsy forceps

Examination of Pleural Fluid Aspiration of a pleural effusion and subsequent microscopy may reveal malignant cells Pleural fluid may be replaced with air to permit of direct inspection of the pleural surfaces at thoracoscopy

Lymph Node Biopsy Biopsy of enlarged supraclavicular nodes if such are present provides a ready means of confirming the diagnosis Their presence however is an indication of inoperability

Aspiration Biopsy or Needle Biopsy This is valuable for peripherally situated tumours It carries the risk of pneumothorax empyema and dissemination of malignant cells and is advised only in obviously inoperable cases in order to confirm a hopeless prognosis or to indicate the histological type for purposes of assessing the chances of temporary improvement from radiotherapy

Exploratory Thoracotomy If all other procedures have proved inconclusive thoracotomy may be performed as a diagnostic measure the surgeon proceeding to resection if the diagnosis is confirmed and the growth technically removable

Complications. Intrathoracic complications are due to local spread of the neoplasm to the pleura or mediastinum Spontaneous pneumothorax dry pleurisy pleural effusion or empyema may develop and occasionally the chest wall and ribs may be directly invaded Mediastinal invasion and lymph node enlargement may cause paralysis of the recurrent laryngeal or phrenic nerves superior vena caval obstruction or dysphagia Pericarditis with or without effusion is sometimes seen late in the disease and various cardiac arrhythmias may follow direct invasion of the cardiac walls Spontaneous venous thrombosis at a distant site is the occasional harbinger of a bronchial carcinoma as it is of malignant growths in other situations

Clubbing of the fingers and toes is frequent especially in cases with secondary pulmonary infection In some however an acute or chronic polyarthritis similar in appearance to rheumatoid disease is seen and may be the first manifestation

The peripheral joints are usually involved with *painful swelling* periarticular oedema and periosteal thickening of the ends of the long bones (hypertrophic pulmonary osteoarthropathy) Its cause is unknown but dramatic relief of the joint symptoms may follow removal of the tumour denervation of the hilum of the lung or even vagotomy Symptoms arising from local metastases in bone are not uncommon and include persistent backache and spontaneous fractures

Involvement of the central nervous system is not infrequent and the earliest signs of the disease may be referable to metastases in the brain The evidence may suggest a localized cerebral tumour or wide spread meningeal and brain involvement Cases are found however in which the clinical picture of cerebellar degeneration is seen but no metastases are present in the cerebellum at autopsy A peripheral neuropathy of sensory motor or mixed type is a well recognized complication and occasionally a non specific myopathy is seen

Prognosis Surgical resection is feasible in only about 12 per cent of cases The average duration of life of inoperable cases is 6 to 9 months although *exceptional cases survive two or three years Even* in apparently resectable cases recurrence is common within 18 months of operation and only 20–30 per cent of patients so treated survive five years

Treatment (*a*) *Preventive* The little that is known of the aetiology is all that prevention can be based upon Young adults should be advised against smoking particularly cigarette smoking It is not *easy to convince them of the long latent period of* some 20 years but the attempt should be made Statistics suggest that even the long standing smoker can lesson his risk by breaking the habit Regular *chest radiography for all adult smokers over the* age of 40 yr has been advocated but this would have to be done every three months in order to improve the prognosis significantly by early detection of the disease This is impracticable for the population as a whole but it should be advised for any workers in occupations already noted as carrying added risk

(*b*) *Curative* Radical surgical resection offers the only chance of cure This usually means a pneumonectomy but lobectomy is sometimes adequate Assessment of operability is the province of the thoracic surgeon but cases with vocal cord or diaphragmatic paralysis superior vena caval obstruction pleural effusion or extrathoracic extension of the disease are unsuitable for radical excision The general condition must also be considered since many of these patients are elderly and suffering from chronic bronchitis or cardiac insufficiency

(*c*) *Palliative* Surgery also plays a part in palliation Removal of a suppurating segment or lobe or the drainage of an empyema may be justified to *improve the general well being if only temporarily* Surgical relief of the arthropathy also has already been mentioned Radiotherapy is of considerable value in alleviation of the more distressing symp*toms of venous obstruction severe cough* pain or dysphagia and in some cases may control the disease for several months Cytotoxic agents are under extensive trial but few cases seem to benefit with *those at present available*

Purely symptomatic treatment may be all that is possible Unnecessary restrictions in the patient's activities should be avoided Pleural effusion may *require aspiration and pulmonary* infection may be helped by a course of antibiotics Euphoriants and effective analgesics should be freely given in an attempt to keep the patient as contented and free *from discomfort* as possible during the few months of life remaining to him

Secondary Neoplasms in the Lungs

The lungs are a common site for metastases as malignant cells may reach them from a distance either by the venous blood stream direct or through *the lymphatics and subclavian vein The primary* growth may be anywhere in the body so that a chest radiograph should be taken before radical surgical treatment is undertaken for any malignant *neoplasm* The commoner primary growths which may metastasize to the lungs are those arising in the breast bronchus kidneys testicles and prostate Chorionepitheliomas and sarcomas also frequently *do so*

Pulmonary metastases may produce no symptoms even when large They appear on radiographs as more or less spherical opacities and are often multiple (*see* Plate 16 14) Metastases from primaries in the testicles and kidneys tend to be solitary or few in number and to reach a large size (cannon ball secondaries) those from the prostate breast and female pelvic organs are often numerous and of smaller size Symptoms depend on the extent of the disease but progressive dyspnoea obstinate cough haemoptysis and pleural pain may all develop before the terminal stages of the disease

Although the condition is fatal considerable relief of symptoms and prolongation of useful life is possible by palliative radio therapy for the more radio sensitive types of neoplasm and appropriate hormone treatment for cancers of the breast and prostate

THE MEDIASTINUM

"The Mediastinal Syndrome'

By simple compression or neoplastic infiltration of neighbouring structures a space-occupying lesion in the mediastinum may give rise to a series of symptoms and physical signs known collectively as the mediastinal syndrome Not all the manifestations are present in each case and indeed a mediastinal mass can be present without producing symptom or sign but often the evidence is unmistakable Clinical features are sometimes sufficiently distinctive to allow of an exact diagnosis but further investigations are often necessary before the nature of the mass can be decided The effects of involvement of the various structures are as follows—

Venous Obstruction distension of the cervical veins and enlarged anastomotic veins coursing downwards over the front of the thorax a sense of fullness in the head and headache is accompanied by a suffused bloated appearance and often oedema of the face neck, and arms (*see* Plate 16 14)

Trachea and Main Bronchi stridor dyspnoea a brassy cough and pulmonary atelectasis

Oesophagus dysphagia

Phrenic Nerve hiccough or paralysis of the hemidiaphragm

Left Recurrent Laryngeal Nerve hoarseness of the voice

Sympathetic Chain Horner s syndrome of ipsilateral ptosis miosis and absence of facial sweating

Arteries partial occlusion of one or other subclavian artery may produce inequality of the radial pulses

Pericardium a pericardial rub or signs of an effusion

Bones erosion of the spine or sternum giving rise to constant severe aching or boring pain

The numerous conditions which may present as a mediastinal tumour may be grouped as follows—

1 *Lymph Node Enlargement*
   - Hodgkin s disease and other lymphomas
   - Lymph node metastases
   - Leukaemia (especially lymphatic)
   - Tuberculous adenitis
   - Sarcoidosis

2. *Retrosternal Goitre*

3 *Neurogenic Tumours*
   - Neurofibroma
   - Ganglioneuroma

4 *Teratoid Tumours*
   - Dermoid
   - Teratoma

5 *Cysts*
   - Bronchogenic
   - Pleuro-pericardial
   - Parasitic (hydatid)

6 *Thymic Tumours*
   - Thymoma

7 *Connective Tissue Tumours*
   - Fibroma
   - Lipoma
   - Myxoma
   - Sarcoma

8 *Miscellaneous Tumours*
   - Aortic or innominate aneurysm
   - Dilated left auricle (mitral stenosis)
   - Tuberculous abscess in relation to the spine
   - Megaoesophagus (achalasia)
   - Diaphragmatic hernia

Differential diagnosis may be extremely difficult. Expert radiography is a first essential for accurate localization of the mass A lateral view is of great value as some lesions occur typically in certain sites. Thymomas and teratoid tumours are usually situated anteriorly neurogenic tumours are mostly in the posterior mediastinum bronchogenic and pericardial cysts are usually in a central position as seen on the lateral film and lymphadenopathies produce a perihilar shadow Additional information is provided by calcification within the mass as the more likely probabilities are then tuberculous adenitis or abscess a teratoid tumour hydatid cyst, or sub sternal colloid goitre Cardiac and aortic lesions are usually evident from their other clinical features The blood count establishes leukaemia and the adenopathy of tuberculosis and of sarcoidosis can usually be distinguished with reasonable certainty by full clinical and laboratory investigation Cervical lymph node biopsy is of great assistance in the diagnosis of cases with primary or secondary malignant lymphadenopathy Bronchoscopy should be carried out if there are no palpable cervical nodes provided aortic aneurysm can be excluded as bronchial carcinoma with lymphatic spread is one of the commonest causes of a mediastinal mass Where no diagnosis can be made thoracotomy is advisable and excision of the tumour if possible Radiotherapy is the best treatment for the lymphomas and the secondary carcinomas

Mediastinal Emphysema (*see* p 358)

Mediastinitis

Acute Mediastinitis This is uncommon but occurs occasionally by direct spread of infection from neighbouring structures or following rupture of the

oesophagus It is associated with severe pain, symptoms and signs of an acute infection and features of the mediastinal syndrome Treatment consists of appropriate antibiotics in large doses surgical drainage and early repair of the gullet

Chronic Mediastinitis Chronic infection of the mediastinum has been described in association with tuberculous adenitis syphilis and actinomycosis An idiopathic form of chronic fibrous mediastinitis is characterized by the slow development of superior vena caval obstruction The chest radiograph may be normal but pathologically there is a dense fibrosis rendering identification of the normal structures almost impossible Surgical treatment is therefore impracticable As the process extends but slowly an adequate collateral circulation may develop and enable the patient to live for many years in comparative comfort

THE DIAPHRAGM

Diaphragmatic pleurisy may have the same aetiology as pleurisy in general (*see* p 361) and may accompany subphrenic infections especially on the right side Subphrenic abscess or amoebic liver abscess commonly declare their presence by symptoms attributable to diaphragmatic pleurisy These are pain in the lower chest or upper abdomen and pain referred to the tip of the shoulder a pleural rub may become audible and a pleural effusion may follow Differential diagnosis and treatment are those of pleurisy as already discussed on p 361 *et seq* Some restriction of movement and distortion of the normal convex contour of the diaphragm may persist after the inflammation has subsided and the normal costophrenic and cardiophrenic angles may be obliterated

Displacement of the Diaphragm

Raised intra abdominal pressure due to obesity ascites pregnancy and large abdominal cysts or tumours causes elevation of the normal diaphragm Diminution in lung volume by atelectasis pulmonary resection or extensive lung fibrosis has the same effect but is usually unilateral Conversely in emphysema the diaphragm is depressed to a low level and flattened

Diaphragmatic Paralysis

In thin subjects a paralysed diaphragm can sometimes be detected clinically by tidal percussion but the diagnosis is most readily made by radioscopy The features are elevation and absence of movement or paradoxical movement well seen during sniffing Unilateral paralysis produces no obvious dyspnoea and although the diaphragm is responsible for about a third of the vital capacity even bilateral paralysis may be present with little dyspnoea at rest provided the other respiratory muscles are normal Flatulent dyspepsia is sometimes attributable to paralysis on the left side

The nerve supply to the diaphragm from the 4th cervical root via the phrenic nerve may be interrupted in a variety of ways Surgical division or crushing of the nerve in the neck in the treatment of pulmonary tuberculosis used to be a common cause Involvement of the nerve by neoplastic infiltration in the mediastinum is also common and is usually due to bronchial carcinoma The anterior horn cells may be affected by poliomyelitis or progressive muscular atrophy or the nerve roots be compressed in tuberculosis of the spine Various forms of polyneuritis including diphtheria may affect the phrenic nerve and occasionally paralysis results from trauma to the neck and is also sometimes a temporary feature accompanying diaphragmatic pleurisy Not infrequently paralysis of a hemidiaphragm is discovered accidentally when no cause can be found

Eventration of the diaphragm is a condition in which there is marked elevation of one side of the diaphragm almost always the left with complete atrophy of the muscle so that only a thin sheet of fibrous tissue remains Some cases are congenital but others result from longstanding phrenic paralysis At first sight the condition suggests a diaphragmatic hernia and a diagnostic pneumoperitoneum may be required for differentiation

Hiccough

Hiccough is produced by a combination of a sudden contraction of the diaphragm and closure of the glottis Its cause is often obscure but temporary spasms are very commonly due to gastric irritation or over distension Alcohol spiced foods a heavy meal rapidly eaten and aerophagy are familiar causes In some cases however hiccough is a manifestation of more serious disease and may be very persistent It may occur with diaphragmatic irritation from peritonitis or pleurisy meteorism uraemia and after abdominal operations It may be a symptom of encephalitis cerebral tumour or hysteria and occasionally epidemics occur in which no cause can be found

Treatment The minor forms of hiccough usually cease spontaneously after some minutes The attack may be terminated by holding the breath drinking iced water or by an alkaline carminative mixture such as *Mist Mag Carb Aromat* (N F) ½ oz

More severe attacks may be extremely difficult to relieve and no single remedy is always effective Treatment is directed to the associated disease when possible Gastric lavage is sometimes effective voluntary hyperventilation or hyperventilation produced by inhaling 7 per cent carbon dioxide in 93 per cent oxygen will often break the vicious circle Simple sedation may be tried and chlorpromazine 25–50 mg 3 or 4 times daily is a useful remedy in obstinate cases Other measures of value include hyoscine hydrobromide 0 3–0 6 mg (1/200–1/100 gr) morphine 10–15 mg (⅙–¼ gr) and interruption of the phrenic nerve The latter can be achieved temporarily by an ethyl chloride spray on to the root of the neck by procaine injection or by phrenic crush

Diaphragmatic Hernia

Traumatic Crushing injuries of the abdomen or lower part of the chest and penetrating wounds may rupture the diaphragm and permit some of the abdominal contents to enter the thorax. The condition may not be noted for a considerable period after the initial trauma as the injury to the diaphragm may be obscured by other injuries Symptoms of dyspnoea and pain may be absent mild or severe and the only treatment is by surgical repair

Non traumatic Congenital diaphragmatic hernias occur through the various apertures normally present in the diaphragm or through foramina resulting from incomplete development The common sites are the oesophageal hiatus the pleuroperitoneal hiatus (foramen of Bochdalek) the foramen of Morgagni and through a congenital defect in the dome of the diaphragm Acquired non traumatic hernias occur through one or other of these apertures most frequently the oesophageal hiatus

Clinical Picture The symptoms are very variable Large congenital hernias can cause severe respiratory embarrassment and cyanosis in newborn infants Otherwise the symptoms if any are chiefly due to oesophagitis and are considered on p 176

Industrial Diseases of the Lungs

THE PNEUMOCONIOSES

In a great many occupations the inhalation of considerable quantities of dust is inevitable Some of these dusts are apparently innocuous but others produce pathological changes in the lungs The official definition of pneumoconiosis in the National Insurance Act is fibrosis of the lungs due to silica dust asbestos dust or other dust including the condition of the lungs known as dust reticulation Silicosis coal miner s pneumoconiosis and asbestosis are the most important forms of occupational pulmonary fibrosis but there are many other dusts capable of producing similar changes Often the dust contains several constituents including a proportion of free silica or silicates and it is sometimes impossible to decide which is the particular noxious agent.

Silicosis

Definition Generalized nodular fibrosis of the lungs due to the inhalation of silicon dioxide

Aetiology Silicon dioxide is widely distributed in nature as sand quartz and flint Only particles of silica of less than 10μ diameter can reach the alveoli by inhalation and it is these which lead to silicosis All occupations in which silica bearing rock has to be worked by drilling crushing or blasting carry a risk of silicosis *e g* the mining of gold copper tin iron slate and coal Other occupations exposing the workmen to similar risk include metal grinding pottery making tunnelling stone dressing fettling boiler scaling and the manufacture of silica bricks or abrasive powders The severity of the lung damage depends upon the concentration of the dust particles and the length of exposure The disease is seldom recognizable in under 10 years exposure but where dust control is inadequate it may develop within two years

Pathology The dust particles are removed from the alveoli by phagocytes and transferred to the perivascular and peribronchial lymphatics Aggregations of the dust are deposited in the lymph follicles throughout the lungs beneath the pleura and in the hilar nodes Wherever the particles lodge a fibrous tissue reaction ensues with the development of concentric whorls of hyaline collagen fibres (silicotic nodule) These increase in size gradually to 5 or 10 mm in diameter and in advanced cases may coalesce to form much larger masses of scar tissue The lung in between the nodes becomes emphysematous and pulmonary function may be severely restricted Additional changes of complicating tuberculous infection are not infrequent

Clinical Picture The onset is insidious and radiographic changes may be apparent before any disability is admitted Gradually increasing dyspnoea is the main symptom with some cough and mucoid sputum probably attributable to the chronic bronchitis which is often present in addition As the disease progresses dyspnoea increases and the

general health deteriorates with lassitude anorexia sometimes haemoptysis and loss of weight Examination of the chest frequently shows no abnormal signs even in quite advanced cases Chest expansion is diminished and the signs of chronic bronchitis and emphysema may be present in variable degree In advanced cases signs suggesting pulmonary tuberculosis may be found or the clinical picture may be that of congestive heart failure

Radiography of the chest shows diffuse mottling or nodulation throughout both lung fields The individual lesions are well-defined roughly circular opacities and the over all appearance has been likened to a snowstorm (Plate 16 15) In later stages the opacities increase in size by confluence and the changes due to superadded tuberculosis may be manifest

Diagnosis The combination of radiographic changes and a clear occupational history are essential for diagnosis It may be necesary to seek the details of previous employment its exact nature and the working conditions The importance of establishing thereby the possibility of silicosis cannot be over stressed since the radiographic appearances alone are not diagnostic A similar appearance is given by many other conditions such as miliary tuberculosis sarcoidosis carcinomatosis haemosiderosis etc as well as other dust diseases

Course and Complications Uncomplicated silicosis is compatible with many years of life and reasonably good health The rate of progress of the disease depends upon the concentration of respirable dust in the atmosphere Cases proving fatal in under two years are described but in most cases the disease does not appear until after 10 years exposure In some cases deterioration may continue after exposure to the dust has ceased The victims do not seem to be predisposed to non specific respiratory infections but take longer to recover from them The main complication is pulmonary tuberculosis which may supervene at any stage its incidence being highest in advanced cases The prognosis of silico tuberculosis was very grave before anti tuberculous drugs were available but has been improved as a result of long term chemotherapy

Treatment. (*a*) *Preventive* Every effort must be made to reduce dust formation to a minimum In the various mining operations steps should be taken to keep the material damp during drilling cutting shovelling or tipping Where possible in industry silica should be replaced by less harmful materials and improved mechanization of the more dangerous occupations be employed where feasible Efficient exhaust ventilation is essential respirators are unreliable and cannot be tolerated by men doing heavy manual work Regular chest radiographs should be taken of all workers at risk There is experimental evidence that inhalation of aluminium dust affords some protection against silicosis but its value in prophylaxis is not yet certain

(*b*) *Symptomatic* The changes in the lungs are permanent and no curative treatment is available The sufferer should be informed that he is entitled to claim compensation for any disability and that his claim will be considered by a Pneumoconiosis Panel of the Ministry of Pensions and National Insurance A change of occupation is advisable for men not too old to learn a new trade General treatment as for chronic bronchitis and emphysema is required and considerable symptomatic benefit can be achieved by regular anti spasmodics and breathing exercises Acute respiratory infections should be treated early with antibiotics Periodic medical examination including sputum tests should enable the onset of pulmonary tuberculosis to be detected early and intensive treatment for this complication with anti bacterial drugs should then begin In advanced stages of the disease appropriate measures for heart failure may also be required

Coal workers' Pneumoconiosis

In the British Isles the commonest and most important form of pneumoconiosis is due to the inhalation of coal dust The disease is most prevalent in the anthracite mines of South Wales workers at the coal face show the highest incidence but firemen shotsmen hauliers and underground labourers in the pits are also affected The same disease is found also in coal trimmers who load ships with coal Signs of the disease seldom appear in under 15 years exposure Coal dust contains not only carbon but some free silica and silicates and the relevant importance of the different constituents in producing the characteristic pathological changes in the lungs is not known A small proportion of coal miners whose work entails rock drilling and cutting in order to expose the coal seams develop typical silicosis but the commoner type of pneumoconiosis affects those actually working the coal and it shows certain differences from pure silicosis

Pathology The coal dust is removed from the alveoli by phagocytes and deposited around the small bronchioles The degree of fibrosis which follows is very much less than that evoked by silica and the concentric nodular pattern is not seen An irregular delicate network of reticulin fibres forms round the coal foci (dust reticulation) and the neighbouring alveoli become dilated possibly as a result of partial bronchiolar obstruction and air trapping This focal emphysema around the black dust deposits is a striking feature In a proportion

of cases a slowly increasing fibrosis develops particularly in the upper lobes with coalescence of lesions to form large irregular masses of tough fibrous tissue (progressive massive fibrosis ') The centres of these lesions may necrose with the formation of an inky black fluid which may be expectorated (melanoptysis) leaving a ragged cavity The exact cause of these lesions is uncertain but there is strong evidence to suggest that secondary tuberculous infection is responsible The condition once established tends to progress regardless of further exposure to coal dust and even if tuberculosis does not become apparent gross distortion of the lungs and impairment of respiratory function lead to right heart failure

Clinical Picture The initial symptom is dyspnoea of gradual onset sometimes with cough producing a little mucoid sputum which is often black in colour The sudden expectoration of a large quantity of black fluid is characteristic of progressive massive fibrosis Progress of simple pneumoconiosis is only slow and any rapid worsening of symptoms suggests superadded pulmonary tuberculosis or other pulmonary disease

Clinical examination of the chest in the early stages may detect no abnormality In the course of time respiratory excursion is diminished and signs of emphysema with some bronchitis appear Localized signs of impaired note altered breath sound and râles suggest pulmonary tuberculosis or other complication

Radiography is essential for early diagnosis The characteristic appearance is of numerous minute opacities of 0 5–2 0 mm in diameter in the lung fields with fine linear shadows connecting them together to form a reticular pattern The changes are seen especially in the middle zones and the lesions are at first relatively sparse As the disease progresses they become larger more profuse and widely scattered in both lung fields but tend to spare the apices Conglomerate shadows of progressive massive fibrosis are commonest in the upper lobes cavitation may be evident within them and as they develop considerable pulmonary fibrosis and contracture with compensatory emphysema becomes apparent

Course and Prognosis The pulmonary changes are permanent but do not progress unless exposure to coal dust continues The early stages are compatible with a normal life span but the possibility of the development of massive fibrosis adds an element of uncertainty to the prognosis Once this appears it progresses slowly regardless of continued exposure to severe disability and ultimate death from right heart failure or tuberculosis

Treatment. Treatment is essentially the same as that discussed under silicosis There can be no substitute for dust suppression in the mines Only palliative treatment is available for those with established disease

Asbestosis

Asbestos is a fibrous mineral containing several silicates and the inhalation of its fibres can produce a severe interstitial pulmonary fibrosis The main lesions are in the respiratory bronchioles where the inflammatory response to the presence of asbestos fibres produces a marked peribronchial fibrosis The lower lobes are particularly involved and considerable pleural thickening is also a feature

Clinical Picture As in other pneumoconioses the initial symptom is dyspnoea followed by cough and mucoid sputum The severity of symptoms parallels the stage of the disease and cyanosis and clubbing of the fingers are seen more commonly in this form of pneumoconiosis Asbestos bodies may be found in the sputum Chest radiographs show a diffuse haziness in the lower halves of the lung fields with no nodulation The outlines of the diaphragm and heart are blurred the upper zones may show emphysema and pleural thickening may be visible

The disease may be complicated by pulmonary tuberculosis but its incidence is less than in silicosis Bronchial carcinoma is undoubtedly more common in sufferers from asbestosis being found in 16 per cent of cases at post mortem

The principles of treatment and prevention are essentially the same as for other dust diseases Since its recognition preventive measures in the industry have reached a high standard and new cases are very rare

Other Noxious Mineral Dusts

Silicates Asbestos is not the only harmful silicate when inhaled into the lungs Talc Fuller s Earth mica china clay etc can produce pulmonary fibrosis similar to that seen in coal miners

Graphite The naturally occurring crystalline form of carbon is mixed with variable quantities of silica A disabling form of pneumoconiosis similar to that produced by coal dust has been described among the workers but it is not known which component of the dust is responsible

Manganese Beryllium Cadmium Osmium and Vanadium The dust or fume of these metals and their compounds are pulmonary irritants Workers in these industries have an increased tendency to bronchitis and higher incidence of pneumonia In addition a delayed reaction has been observed in beryllium workers employed in the manufacture of fluorescent lamps in which zinc beryllium silicate is

used The lung lesions closely resemble sarcoidosis but are only part of a more generalized reaction since granulomas are found in lymph nodes spleen and liver The condition may only develop some months or even years after contact with beryllium has ceased

Arsenic Chromates Nickel and Radio active Ores The association of bronchial carcinoma with these industries has already been noted (p 371)

Iron Tin and Barium Inhalation of metal fume or oxides of these metals does not induce any fibrous tissue reaction in the lungs but because they are radio opaque they may produce extensive radio graphic changes of a nodular character indistin guishable from silicosis *Siderosis* is the commonest member of the group and is not uncommon in welders and oxyacetylene cutters Silver polishers may show similar changes from the use of rouge The condition produces no disability and the sha dows may fade slowly if exposure ceases

Noxious Vegetable Dusts

In discussing chronic bronchitis the opinion was expressed that dusty atmospheres and occupations were deleterious and tended to aggravate the dis ease in patients already prone to it Bronchitis has been reported in men exposed to many kinds of vegetable dust including that from flour flax hemp tea and cotton The mode of action is uncertain some believing that an allergy to the dust develops others that it is simply a question of mechanical irritation Although there can be little doubt that chronic bronchitis is adversely affected by smoke and dust it is much more difficult to prove a causal relationship In certain instances however the evi dence is unmistakable

Byssinosis

This is a form of chronic bronchitis and emphy sema which affects workers exposed to cotton dust Those engaged in the carding and spinning of cotton are particularly affected the disease appearing only after several years exposure At first the symptoms of cough dyspnoea and wheezing appear only at the beginning of the week (Monday morning fever ') and rapidly subside to return again at the beginning of the next week exposure having ceased over the week end The symptoms gradually worsen becom ing more persistent and lasting throughout the week but still relieved over the week end away from the factory Ultimately the chronic stage is reached when the symptoms are permanent and the clinical features are those of chronic bronchitis and emphy sema Pulmonary fibrosis does not occur The chest radiograph is normal early in the disease and in the advanced stage shows only emphysema Recovery is possible if the occupation is changed before the symptoms have become permanent Symptomatic treatment is the same as for chronic bronchitis

Bagassosis

Dried sugar-cane after the extraction of the sugar is known as bagasse and in addition to the vegetable fibres it contains amorphous silica and various fungi It is used in the manufacture of fibre boards Workers exposed to bagasse dust for periods of weeks or months may develop a bronchopneu monia with fine or coarse inflammatory foci in the lungs A more chronic form of the disease not unlike byssinosis with the features of chronic bron chitis is also encountered Which constituent of the dust is responsible is unknown The disease can be prevented by working bagasse only in the damp state and any worker showing symptoms should cease this occupation

Farmers Lung or Threshers Lung

This is a pulmonary disease affecting harvest workers due to the inhalation of dust during hay making or threshing of grain Such dust contains many fungi which may in some way be the cause of the disease In some cases the onset is rapid with fever and signs of bronchitis In others it appears more gradually with increasing dyspnoea produc tive cough clubbing of the fingers and cyanosis Chest radiographs at the start show reticulation or soft mottling but in the more chronic stages patchy atelectasis fibrosis and emphysema If further exposure is avoided the patient will recover from the early stages Potassium iodide is of value in treatment but in progressive cases irreversible changes in the lungs occur and may lead to heart failure

Miscellaneous Pulmonary Diseases

Sarcoidosis

Definition A chronic disease of unknown aeti ology characterized by a granulomatous infiltration of many organs Its general features are considered on p 165

Pulmonary sarcoidosis is one of the commonest manifestations of the disease

Bilateral hilar lymphadenopathy is usually the first intrathoracic manifestation (*see* Plate 16 16) It is generally symptomless but in some cases ery

thema nodosum and arthritic pains occur at the same time The nodes may subside completely without any apparent change in the lungs In some cases however as the nodes subside a generalized fine or coarse mottling appears in the lung fields This increases over a period of months and having reached its maximum may then slowly clear and resolve completely the patient having had no respiratory symptoms throughout In other cases however resolution does not occur and eventually a coarse pulmonary fibrosis and emphysema result At this stage increasing dyspnoea is evident and right heart failure may supervene

Differential Diagnosis. A variety of clinical conditions may be simulated by sarcoidosis For practical purposes the most important are the various painless lymphadenopathies *e g* Hodgkin s disease leukaemia and malignant disease the several causes of diffuse fine or coarse shadows in the lungs e g pulmonary congestion pneumoconiosis carcinomatosis and certain types of pulmonary tuberculosis Histological confirmation is often necessary It should be noted however that distinction from tuberculosis is sometimes extremely difficult and cases are met in which the two diseases seem to merge one into the other

Prognosis of the Pulmonary Lesions Cases presenting with erythema nodosum and hilar lymphadenopathy have a good prognosis and usually recover without any treatment In the stage of pulmonary infiltration it is impossible to give an accurate forecast About 50 per cent of these cases after remaining apparently stationary for many months will clear slowly and resolve completely Some of the others remain unchanged for years without symptoms but a proportion of them progress to extensive pulmonary fibrosis with secondary emphysema Disability in this type is severe and a fatal outcome is frequently due to right heart failure or pulmonary tuberculosis

Treatment. The substances which most reliably influence the disease are the steroid hormones The decision whether to give them when there are pulmonary lesions is difficult since spontaneous remission is common Close radiographic observation is advisable and steroids should be given only to those showing radiological deterioration to those failing to show spontaneous improvement after a period of six to nine months and to those with lesions sufficiently extensive at the time of diagnosis to produce symptoms. In advanced cases with extensive pulmonary fibrosis no permanent benefit results although some symptomatic improvement may be achieved Unfortunately a favourable initial response may be followed by relapse In such the treatment should continue for at least a year Oral cortisone 100–150 mg per day reducing to a maintenance dose of 75 mg per day is effective but prednisolone 15–20 mg daily is superior in producing fewer side effects Concurrent administration of anti tuberculous drugs is unnecessary in most cases though they are still given as a precautionary measure by some physicians when a tuberculous aetiology seems likely

Lung Lesions in the Collagen Diseases

Pleural and pulmonary lesions are not uncommon in the group of conditions known as the collagenoses They may be overshadowed by the general systemic manifestations but sometimes dominate the clinical picture and may precede other lesions by months or even years

Polyarteritis Nodosa

In most cases the lungs are spared but in 20 per cent of cases an intractable form of asthma develops Haemoptysis and pleural pain may occur due to pulmonary infarction The radiographic changes are of considerable variety and not in themselves specific Transient infiltration or more persistent coarse miliary or nodular shadows are the usual findings Larger confluent shadows are seen in some cases and represent areas of non infective pneumonia infarction or pulmonary oedema and a pleural effusion may form

Systemic Lupus Erythematosus

The commonest intrathoracic lesions in this disease are pleural and pericardial effusions A chronic interstitial pneumonia with atelectasis is also described

Scleroderma

The lungs may be affected in the more severe cases producing a dry cough and progressive dyspnoea A diffuse pulmonary fibrosis especially affecting the lower lobes is the usual finding and radiographically a fine nodulation or cystic appearance may be seen These patients are also more susceptible to ordinary pulmonary infections

Rheumatoid Arthritis

Pulmonary and pleural lesions may complicate rheumatoid disease but are uncommon Parenchymal infiltration associated with cough dyspnoea

and fever may occur relatively early in the disease and tends to coincide with acute exacerbations of the arthritis Pleural effusion and subpleural nodules histologically the same as the subcutaneous nodules are also found and tend to develop in long standing cases often when the joints are quiescent

Pulmonary Diseases due to Fungi and Parasites

Parasitic and fungal diseases of the lungs are quite rare *in this country* *The commoner varieties* are enumerated below but for detailed descriptions more specialized textbooks must be consulted

Fungal	*Organism*
Histoplasmosis	*Histoplasma capsulatum*
Coccidioidomycosis	*Coccidioides immitis*
Moniliasis	*Candida albicans*
Aspergillosis	*Aspergillus fumigatus*
Actinomycosis	*Actinomyces bovis*
Torulosis	*Cryptococcus neoformans*
Blastomycosis	*Blastomyces dermatitidis*

Parasitic	*Organism*
Amoebiasis	*Entamoeba histolytica*
Malaria	*Plasmodium falciparum*
Hydatid cyst	*Echinococcus granulosus*
Schistosomiasis	Various types of *Schistosoma*
Paragonimiasis	*Paragonimus westermani*

Pulmonary Embolism and Infarction

Definition Pulmonary embolism is the sudden obstruction of the lumen of the pulmonary artery or one of its branches by abnormal material usually blood clot Pulmonary infarction refers to the pathological changes which may follow arterial obstruction but these are not invariable

Incidence Males and females are affected equally *with the exception of fat embolism* which is more common in males It occurs in elderly subjects particularly and is rare before the age of twenty Approximately 2–3 per cent of all deaths and between 5–10 per cent of post operative deaths are attributable to it One third to one half of all patients dying from mitral stenosis or congestive heart failure shows pulmonary emboli at autopsy

Aetiology As a rule emboli consist of uninfected blood clot which has formed in and been detached *from one of the systemic veins usually in the* calves The pelvic and other veins are sometimes the site of the primary thrombosis In auricular fibrillation the blood clot may derive from the right auricle or rarely infective endocarditis affecting the right side of the heart may be the source A few cases result from primary pulmonary thrombosis during the course of *mitral stenosis* congestive heart failure or primary arterial disease e g polyarteritis nodosa Emboli are occasionally composed *of septic material* tumour cells parasites air or fat globules The common type varies greatly in size and is often multiple Infarction is more likely to follow the larger emboli particularly in patients already suffering from pulmonary congestion

Predisposing Factors Immobility particularly of the legs predisposes to venous thrombosis If the venous *return is no longer* aided by muscular contraction stasis occurs and may be increased mechanically by the *orthopnoeic position* Diminished respiratory excursion is another important factor in decreasing venous return the pain following abdominal operations tight abdominal binders and obesity are all important from this point of view Other factors which play some part are dehydration shock toxaemia and excessive manipulation of viscera at operation *In addition after* surgical operations there are certain changes in the blood which allow it to clot more readily The fibrinogen the prothrombin activity the number of platelets and the E S R all increase to a maximum in the second post operative week In individual cases various combinations of these many factors culminate in the initial phlebo thrombosis

Pathology The lungs of patients who have died suddenly from massive pulmonary embolism appear *normal A large or long coiled thrombus* is found in the pulmonary artery or its main branches but unattached to the walls When infarction has occurred the area is dark red in colour and firm in consistency The affected portion of lung is airless the alveoli being filled with oedema and red cells Infarcts are typically wedge shaped with an area *of pleurisy over the base which is situated peri*pherally Often however they are ill-defined A small blood stained pleural effusion is common When the collateral circulation is adequate the alveolar walls remain intact and complete resolution is possible but if inadequate the alveoli undergo necrosis and healing is then by fibrosis Multiple infarcts may be present *in varying degrees* of resolution

Clinical Picture *Massive Pulmonary Embolism* The patient is suddenly seized with an intense constriction in the chest acute dyspnoea and terror

Death may take place within minutes Should he survive the immediate event he presents the clinical picture of shock with pallor sweating cyanosis coldness of the extremities rapid feeble pulse and low blood pressure Signs of acute right heart stress may be evident, *i e* cervical vein engorgement triple rhythm and accentuation of the pulmonary second sound No signs are detectable in the lungs

Pulmonary Infarction Symptoms vary from being very slight to acute distress The commonest symptom is pleural pain causing a catch in the breath and referred to the site of infarction. Dyspnoea may accompany the pain and is sometimes wheezing in type Haemoptysis occurs in about 50 per cent of cases but may not appear for 24-36 hr after the initial symptom The blood is bright red at first, seldom profuse and gradually lessens and darkens in colour over the next few days Tachycardia moderate fever and a leucocytosis are usually present. Cough faintness restlessness cyanosis and variable degrees of shock are seen depending on the size and number of the infarcts

Examination of the chest may reveal no signs if the infarct is small A pleural rub is often heard and there may be an area of weak breath sounds and rales Signs of consolidation or pleural effusion may develop If the legs have been the source of the embolus local tenderness of the calf oedema or pain on dorsiflexion of the foot may be elicited (Homan s sign)

Radiographs of the lungs are normal in cases of massive embolism In cases with infarction a typical wedge shaped opacity is but rarely seen More commonly there is an ill defined shadow in the lower zone with evidence of overlying pleural involvement Larger areas of consolidation or pleural effusion may be present and the diaphragm may be elevated on the affected side Serial radiographs may show progressive resolution from the periphery gradual shrinkage to leave persistent fibrous bands pleural thickening and occasionally if the infarct has been septic softening to form a lung abscess

Diagnosis and Differential Diagnosis Massive embolism closely simulates a coronary thrombosis An electrocardiogram is helpful in differentiation when it shows changes characteristic of acute right heart stress (acute cor pulmonale) The typical clinical features of pulmonary infarction occurring in the second week after a surgical operation cause no difficulty in diagnosis Post operative massive atelectasis occurs in the first few days after operation and haemoptysis is unusual Other conditions which at times may have to be considered are spontaneous pneumothorax acute left ventricular failure and in the less dramatic cases other causes of pleurisy (*see* p 361)

Complications and Prognosis The larger the embolism the more serious the prognosis Massive embolism carries a high mortality from circulatory failure and asphyxia and various cardiac arrhythmias may appear at the onset. The outlook in less severe cases is generally good although the risk of further emboli adds uncertainty to the prognosis Pleural effusion which is sterile and often blood stained is a common complication but is seldom large it may however persist in a chronic form in patients already suffering from pulmonary congestion due to heart disease Unless the embolus itself consists of septic material the infarct rarely becomes infected Repeated infarcts and their subsequent organization may lead to chronic right heart failure

Treatment (*a*) *Preventive* The risk of venous thrombosis should be minimized by counteracting the predisposing factors already discussed Early ambulation should be encouraged for surgical patients and all those confined to bed should be instructed to move their legs about freely and to do deep breathing exercises for regular periods throughout the day Excessive trauma at operation constricting binders and dehydration should be avoided Regular examination of the legs may detect early thrombosis and treatment should then begin before symptoms of pulmonary embolism have occurred The prophylactic use of anti-coagulants should be considered where further surgery is necessary for patients who have previously had venous thrombosis

(*b*) *Curative Treatment* (*a*) Massive Embolism Immediate treatment consists of oxygen and morphine in small doses to allay anxiety and pain Atropine 1 mg (1/60 gr) and papaverine 30–60 mg (½–1 gr) I V are advocated by some in order to combat vagal reflex spasm of the coronary and pulmonary arteries The heroic procedure of embolectomy has saved a few lives and may be considered where facilities are available and where death otherwise seems inevitable Anti-coagulants should begin as soon as the emergency measures have been instituted

(*b*) Pulmonary Infarction The pain and restlessness should be relieved by small doses of morphine or pethidine Oxygen is required if there is cyanosis Penicillin is usually advised to prevent secondary infection but this risk is small a dose of 600 000 units of the procaine salt I.M once daily is adequate Treatment with anti coagulants should begin with heparin 10 000–15 000 units (100–150 mg) I V repeating this dose every 4 to 6 hr for the first 24 hr depending on the clotting time which should be

maintained between 15–20 min Phenindione (Dindevan) should be given by mouth at the onset its effect appearing in 24 hr when heparin can be discontinued The dose of phenindione is 200 mg in the first 24 hr 100 mg in the second 24 hr and thereafter 50–100 mg every 24 hr depending on the prothrombin concentration the aim being to maintain this between 20 and 30 per cent of normal Anti coagulants should be continued to cover the period when the patient begins to get up and about in most cases for three or four weeks If in spite of anti coagulants further emboli occur ligation of the femoral veins or inferior vena cava may be considered

Fat Embolism

Incidence and Aetiology Fat embolism is more common in men than women probably because men are more subject to trauma Autopsies on fatal accident cases show it to be of relatively frequent occurrence although unrecognized clinically It occurs particularly following fractures or severe contusions to adipose tissue Occasionally it results from severe burns manipulative operations and therapeutic injections

Pathology In contrast to a metabolic lipaemia fat globules enter the blood stream probably from the site of injury and are of sufficient size to obstruct the capillaries and cause anoxaemia At post mortem all the organs of the body may be involved The lungs are firm and oedematous and blood stained frothy fluid containing fat globules exudes on pressure Clear wedge shaped infarcts are not seen General signs of asphyxia are present, with petechiae in the white matter on mucous membranes and over the upper part of the trunk

Clinical Picture Symptoms appear within three days of the injury In severe cases the patient may die in a few hours from acute pulmonary oedema More often however symptoms develop and increase more gradually with dyspnoea pallor sweating restlessness cyanosis tightness in the chest and frothy haemoptysis The pulse temperature and respiration are all raised Diminished breath sounds and scattered rales are heard as pulmonary oedema develops and occasionally small areas of consolidation can be detected If the patient survives some of the fat gets through the pulmonary capillaries into the systemic circulation It then causes cerebral symptoms such as disorientation fits incontinence hemiplegia coma and finally death At the same time emboli reach other structures and show as petechiae over the palate conjunctivae and upper part of the trunk Extracellular fat globules may appear in the urine or sputum

Treatment Early and efficient immobilization of injured limbs and minimal transportation reduces the frequency of fat embolism Oxygen is the first essential the patient being placed in an oxygen tent if facial injuries prohibit the wearing of a mask. Atropine and papaverine i v as for pulmonary embolism are worth trying Sodium desoxycholate has been used with limited success in an attempt to emulsify the fat and reduce blood viscosity 10 ml of 20 per cent solution are given i v very slowly every two or three hours Penicillin should be given to lessen the risk of hypostatic pneumonia

Physiotherapy in Diseases of the Chest

Physiotherapy plays an important part in the management of patients with chest diseases Its main objects are two fold—

1 Promotion of adequate drainage of the bronchial tree and
2 Improvement in ventilation of the alveoli

Depending upon the effects of the disease process one or other of these objects will be the more important but in some conditions both are needed Many different diseases require the same type of physiotherapy which is dictated more by the structural and functional derangements than by the disease itself Bronchial drainage is encouraged by the simple use of gravity and this is the basis of postural drainage (*see below*) Improvement in ventilatory function may demand the correction of faulty posture the development and effective use of the muscles of respiration and training in the conscious use of muscles not normally employed for this purpose

Postural Drainage

The principle of postural drainage is to place the patient in such a position that the affected part of the lung can drain via its bronchi towards the tracheal bifurcation The secretions will there excite the cough reflex and be expectorated A knowledge of the main divisions of the bronchial tree and their directions is necessary in order to apply the treatment intelligently and to avoid doing harm by it The positions to be adopted for drainage of the various lung segments are illustrated in Plates 16 12 and 16 13 Expensive apparatus such as a Nelson bed is not essential as with a little ingenuity an ordinary single bed and bed blocks or an impro-

vised wooden frame are quite adequate provided that the principles are understood The inhalation of 1 per cent isoprenaline or similar broncho-dilator before drainage begins will assist the dislodgement of sputum which is further encouraged during drainage by clapping the chest wall by pressure vibrations during prolonged expiration and by instructing the patient to cough Clapping or percussion is avoided when acute inflammatory processes are present or if there has been a recent haemoptysis of any severity

Conditions for which Postural Drainage is Beneficial. *Bronchiectasis* Prior to surgical resection the dilated bronchi should be as free from sputum as possible In patients with irreversible infected bronchiectasis unsuitable for surgery regular postural drainage is necessary to maintain health and prevent complications The extent and distribution of the disease is determined by bronchography and postural drainage planned accordingly The duration of the treatment depends upon the co operation of the patient, the amount of sputum etc but in severe cases the time spent in the position of drainage should be increased gradually up to several hours each day As control is achieved and sputum diminishes the time is reduced to an effective minimum Often 15–30 min twice daily will be sufficient for maintenance the patient being instructed to increase this during an exacerbation of symptoms

Lung Abscess With postural drainage and intensive chemotherapy the majority of lung abscesses recover well The principles are the same as for bronchiectasis although bronchography is seldom required for localization Heavy percussion of the chest is avoided in the early stages in view of the risk of precipitating haemoptysis

Atelectasis As a prophylactic measure whenever possible all bronchitic subjects and heavy smokers should have postural drainage and breathing exercises for several days before a surgical operation to reduce the incidence of post operative atelectasis In the established case postural drainage should begin at once and continue to the point of tolerance along with other measures to assist expectoration (*see* p 329)

Other Conditions Chronic bronchitics particularly during the winter months should practise postural drainage morning and evening It hastens resolution in the convalescent stage of pneumonia especially the common type which is in effect an infected atelectasis Patients with a permanent tracheostomy or paralysis of respiratory muscles and therefore unable to cough up their bronchial secretions should be protected against pulmonary complications by its use In general postural drainage can be applied with benefit to any patient who has an excessive amount of sputum and an ineffective cough

Conditions in which the Main Aim of Physiotherapy is to Improve Pulmonary Ventilation *Asthma* In an acute attack of asthma the patient is unable to co operate in physiotherapy but it is of value between the attacks By its use minor attacks can often be aborted and the tendency to over inflation of the lungs can be corrected the onset of emphysema may be delayed or if already established its rate of progress may be slowed down and the dyspnoea from it may be relieved

Individual instruction is important at first. Asthmatics are often tense frightened people who must first be helped to relax both physically and mentally During this stage a slow rate of respiration is encouraged with the accent always on expiration Deep inspiration is avoided and the patient is gradually taught the conscious control of expiration with employment of the abdominal muscles Light pursing of the lips or hissing during the expiratory phase helps him to grasp the object of these exercises which should be practised morning and evening and at any time that dyspnoea is noticed Mental counting up to two for inspiration and up to four for expiration is another aid in focusing his attention on the necessity to empty rather than fill the lungs more completely Short expiratory breathing exercises in a relaxed posture leaning forward with the arms resting on a table will often abort a minor attack and hasten recovery from effort dyspnoea

Chronic Bronchitis and Emphysema The aim of physiotherapy is similar to that in asthma to decrease the residual air by teaching the patient to empty his lungs more thoroughly by conscious effort Breathing exercises are directed at improving the excursion of the diaphragm and lower part of the chest Many patients also require trunk and shoulder girdle exercises designed to correct postural defects and develop a satisfactory relaxed bearing

Miscellaneous Conditions. During the convalescent stage of acute bronchitis pneumonia and other inflammatory pulmonary conditions physiotherapeutic measures are of assistance in hastening the process of resolution and ensuring that this shall be complete Postural drainage is followed by pressure expansion exercises continued regularly until all sputum has gone and the lungs are radiologically normal

In generalized fibrosis of the lung such as occurs in sarcoidosis and the pneumoconioses the main disability arises from interference with gaseous exchange (alveolar-capillary block) and physiotherapy cannot hope to affect this To some extent however

the dyspnoea is due to contraction of the lungs and diminished elasticity and some improvement can be achieved by exercises designed to increase the chest excursion in both inspiration and expiration Similarly patients with extensive scarring of the chest wall following burns or those with ankylosing spondylitis may be helped to regain some of their lost chest movement

Surgical Conditions The value of pre operative postural drainage and breathing exercises in the prevention of post operative atelectasis in general surgical patients has been noted Physiotherapy is even more important for those about to undergo operations on the chest in order to minimize the effects of paradoxical chest wall movement which follows the resection of ribs Assisted coughing is of first importance with arm and trunk exercises to counteract any tendency to deformity After pulmonary resection expansion of the residual lung is encouraged by localized pressure-expansion exercises against light pressure of the hand or a broad belt. In summary the efforts of the physiotherapist after all these operations are directed towards ensuring bronchial drainage maintaining a mobile thoracic cage and diaphragm increasing the function of the remaining lung and the prevention of deformity Many surgical patients both general and thoracic are elderly and somewhat inactive and although attention may have to be concentrated on the chest, massage and active exercises especially for the lower limbs are advisable in addition in order to discourage venous thrombosis

CHAPTER 17

Diseases of the Nervous System

MICHAEL KREMER

(with section on Poliomyelitis by JOHN FORBES)

Investigation of Neurological Cases

INVESTIGATIONS should be chosen with care after full consideration of the history and clinical examination of the patient They should be regarded as an extension of the clinical examination and should be interpreted in the light of all the other findings An X ray shadow electrical tracing or chemical analysis alone should rarely invalidate a firm clinical diagnosis

Cerebro-spinal Fluid (C.S F)

C.S F may be obtained from the lumbar subarachnoid space or cisterna magna by needle puncture and from the cerebral ventricles by a brain needle after making burr holes in the skull Lumbar or cisternal punctures must be carried out with full aseptic precautions They should not be done if the C S F pressure is felt to be greatly raised or an abnormal space occupying structure is present inside the skull Coning of the cerebellum through the foramen magnum or the temporal lobe through the tentorial hiatus may then occur and urgent neurosurgical intervention may be necessary to save the patient s life

In meningitis and in toxic or otitic hydrocephalus where the pressure is raised free drainage of C S F through the lumbar puncture needle may be allowed and will give much relief

An attempt should always be made to measure the pressure of the C S F by attaching a manometer to the needle If the pressure is within normal limits jugular vein compression should be tried to establish whether or not there is a free flow of C S F along the spinal theca If properly done this manœuvre should cause a rise of C S F pressure to above 300 mm of water in less than 15 sec Once jugular compression is released the pressure should fall to the resting level in a similar time This procedure may be repeated with the neck extended and flexed A real difference between the two results is suggestive of partial cervical spinal compression as by cervical spondylosis

The abnormalities to be found in the fluid in different disorders are described under the respective headings

X rays

(a) Plain X rays of the Skull. Plain X rays of the skull can give a great deal of very valuable information Abnormalities of shape and size of congenital origin are readily seen Oxycephaly or tower skull microcephaly and infantile hydrocephalus are obvious While a mild degree of asymmetry is not unusual marked asymmetry may occur in infantile hemiplegia and localized bulging in the middle cranial fossa will be found in juvenile subdural haematoma

Excessive shallowness in the posterior fossa may be seen in congenital narrowing or atresia of the aqueduct of Sylvius The disorders in the neighbourhood of the foramen magnum are of recent interest These may be congenital or acquired due to bone softening and are given the general label of basilar impression This means that for one reason or another the ring of bone around the foramen magnum rises into the posterior fossa producing compression of its contents Tomograms through the foramen may be necessary to see the condition

Raised intracranial pressure causes separation of the sutures in children and an increase in the digital impressions on the inner table giving the so called beaten silver appearance In adults the most marked changes are erosion or thinning of the clinoid processes deepening of the sella turcica and thinning of the dorsum sellae

Hyperostosis of the inner table of the frontal bone is common in middle aged women and may not be associated with neurological changes but localized hyperostosis can often be found near the origin of a meningioma Changes due to disease of bone are readily seen and include Paget s disease localized osteomas and local and general fibrocystic disease

Calcification occurs in the pineal and choroid plexus in many normal people over thirty Displacement of this normal calcification may help to lateralize tumours Calcification may also be found in an arteriosclerotic carotid especially in its course through the cavernous sinus in abnormal blood vessels such as capillary angiomas (Sturge Weber syndrome) and sometimes in arteriovenous angiomas Tumours such as the gliomas and meningiomas tuberculomas suprasellar cysts haematomas clotted aneurysms and parasites may all calcify

Rarefaction of bone may be due to malignant or lipoid deposits Localized erosion is caused by expanding tumours as in the sella turcica by a pituitary tumour the internal auditory meatus by an acoustic nerve tumour and the *optic foramen* by a glioma of the optic nerve

Abnormalities of vascular markings leading to or from a highly vascular tumour may be seen *Interpreting these findings is difficult as some normal* skulls show very heavy vascular markings

(b) Special X rays Angiography Cerebral angiography is now carried out by the percutaneous *technique A needle is inserted directly into the* carotid or vertebral artery and a radio opaque *substance containing an organic iodine compound* is injected Films in various planes are exposed rapidly and pictures are thus obtained with dye in the arteries arterioles and larger veins By this means partial or complete vascular obstruction can be seen in the carotid or vertebral circulation Care is needed to distinguish spasm from more permanent obstruction

When the circulation is filled displacement of vessels as by tumours cysts or large ventricles can be seen Subdural haematomas prevent the vascular pattern from reaching the inner table of the skull The vessels may show aneurysms and arteriovenous angiomas Vascular tumours show an abnormal vascular pattern such as the blush of the meningioma

Air Encephalography or Ventriculography Air may be introduced into the subarachnoid space by either *lumbar or cisternal puncture with the patient* sitting upright The air rises into the skull frequently *filling the cerebral ventricles* and always filling the basal cisterns By making burr holes in the skull air can be put directly into the ventricles by a brain needle

By these techniques the shape and size of the ventricles can be studied and dilatation by atrophy or obstruction can easily be seen The ventricles may be displaced by tumours or cysts or show filling defects and the subarachnoid cisterns can be prevented from filling by tumours In atrophic conditions the sulci are widened and pooling of cortical air is found

X rays of the Spine Plain X rays of the spine may show developmental abnormalities such as spina bifida fusion of vertebrae (Klippel Feil deformity) or hemivertebrae

Degenerative changes in and around the joints may be seen in spondylosis with osteophyte formation in Charcot joints or ankylosing spondylitis Oblique films to show the foramina may show encroachment by osteophytes Erosion of bone in the foramina may be due to neurofibromas and erosion *of the pedicles with widening of the space between* them may be due to many tumours

Erosion of the posterior surface of the vertebral bodies by tumours and cysts may also be seen *Narrowing of the intervertebral disc spaces is common* in degeneration of the discs though this is *often seen in the cervical region of middle* aged people who are symptom free Many diseases of *bone may produce deformity in the spine and impair* spinal cord function but they cannot *be included here*

Special X rays can be taken of the spine after *radio opaque material such as myodil is introduced* into the subarachnoid space and moved up and *down on a tilting table during X ray screening* This will show obstruction due to tumours cysts and *displaced discs abnormal blood vessels* and nonfilling of the dural sleeve of the nerve roots due to compression in the exit foramen

Electroencephalography

The development of electronic techniques has enabled the normal voltages developed in the brain *to be picked up by scalp electrodes and* magnified sufficiently to be recorded by penwriters on paper *By recording from a number of electrodes* simultaneously the electrical function of different parts *of the brain can be compared* A good deal of experience is needed to distinguish normal variations *from abnormalities*

The normal E E G in adults shows an alpha *rhythm that is a wave cycle* of 8–12/sec of varying amplitude arising posteriorly and spreading symmetrically *forward* though often not reaching the frontal regions this rhythm is best seen when the eyes are shut and the mind at rest and is blocked by opening the eyes

This pattern is disturbed by the occurrence of epileptic waves In grand mal high voltage waves or spikes of high frequency usually symmetrical begin before the clinical attack and go on during the attack In classical petit mal there are 3 c/sec spikes and waves symmetrically over the cortex

In psychomotor attacks 4 to 6 c/sec waves usually occur in the anterior temporal region

These features may however be found only in prolonged recordings Special methods of activation such as over breathing flickering lights sleep or analeptic drugs may therefore be required to show the characteristic pattern Sometimes the ordinary scalp electrodes are insufficient especially when the waves are arising in the inferior surface of the brain Sphenoidal electrodes may then have to be used

Even in idiopathic epilepsy the abnormal waves may seem to be more prominent in one region and phase reversal may occur on either side of this focus Serial records are then needed to show whether this focus moves round the cortex as it may in epilepsy or remains constant as it does when there is a structural abnormality

In the interseizure period no abnormality may be found or a periodic disturbance of the alpha rhythm not absolutely diagnostic of epilepsy may occur Similarly the pattern of a very brief epileptic seizure may be seen in the record of a patient who has no clinical disturbance of any kind

When epilepsy is due to a progressive lesion both epileptic wave forms and evidence of a structural abnormality may be present if the condition is near the cortex Slow waves are seen which spreading out from the focus give a phase reversal in the recording from the electrodes on either side The greater the cortical disruption especially by oedema the greater the E E G changes Naturally serial recordings show evidence of progression The most striking changes are to be found with acute abscesses whereas deep slowly growing tumours may produce very little change

Tumours subdural haematomas and porencephalic cysts which are situated posteriorly may cause a diminution in the amplitude of the alpha rhythm on the side of the lesion

Metabolic disorders such as hepatic pre-coma or uraemia produce profound though transient changes often well in advance of the onset of confusion and drowsiness Similarly transient changes may be due to alterations in electrolytes and acid base equilibrium

Vascular lesions especially if deep seated may not produce dramatic changes In the internal capsule the changes depend upon the amount of surrounding oedema and serial records usually show steady improvement This is important in distinguishing vascular lesions from progressive disorders such as tumours

Electromyography

By using concentric needle electrodes the action currents from muscles can be readily studied In a denervated muscle the number and amplitude of motor units is reduced and very small fibrillation action potentials are seen from about 18 days after denervation until no living muscle fibres remain During recovery new motor units are readily recognized by the biphasic character of the action currents The E M G can help in the study of muscle disorders such as myopathy polymyositis myasthenia gravis and the myelopathies There are recognized differences in the shape frequency and grouping of the motor unit action currents and of the response to full voluntary contraction produced by these various conditions which may be of diagnostic value

The E M G has recently been used to measure the conduction time in motor and sensory fibres in peripheral nerves This is generally delayed in the various forms of neuritis and may be locally delayed by an area of dysfunction as when the median nerve is compressed in the carpal tunnel in the acroparaesthesia syndrome or the ulnar nerve is compressed at the elbow

HEADACHE

Headache is one of the most common symptoms presented by patients in neurological departments While it is frequently a manifestation of relatively minor conditions it can be the leading phenomenon of severe and fatal intracranial disease It has been extensively investigated in man with modern techniques particularly during craniotomy carried out under local anaesthesia and a great deal of information about the basic mechanisms is available

Pain sensitive structures inside the skull are (1) the major venous sinuses and their tributaries from the surface of the brain (2) the meningeal arteries (3) the basal arteries leading to and forming the circle of Willis (4) the dura of the anterior and posterior fossae (but not the middle fossa) of the skull (5) certain sensory nerves such as the trigeminal the glossopharyngeal and the vagus The rest of the intracranial structures such as the cerebral tissue most of the lining membranes the ependyma and the choroid plexuses and the skull itself are insensitive to pain

Pain produced from structures above the tentorium cerebelli is felt in front of the vertical line joining the two external auditory meati *i e* in the trigeminal area Pain from structures below the tentorium is felt behind this line

Calcification occurs in the pineal and choroid plexus in many normal people over thirty Displacement of this normal calcification may help to lateralize tumours Calcification may also be found in an arteriosclerotic carotid especially in its course through the cavernous sinus in abnormal blood vessels such as capillary angiomas (Sturge Weber syndrome) and sometimes in arteriovenous angiomas Tumours such as the gliomas and meningiomas tuberculomas suprasellar cysts haematomas clotted aneurysms and parasites may all calcify

Rarefaction of bone may be due to malignant or lipoid deposits Localized erosion is caused by expanding tumours as in the sella turcica by a pituitary tumour the internal auditory meatus by an acoustic nerve tumour and the optic foramen by a *glioma of the optic nerve*

Abnormalities of vascular markings leading to or from a highly vascular tumour may be seen Interpreting these findings is difficult as some normal skulls show very heavy vascular markings

(b) Special X rays Angiography Cerebral angiography is now carried out by the percutaneous technique A needle is inserted directly into the carotid or vertebral artery and a radio opaque substance containing an organic iodine compound is injected Films in various planes are exposed rapidly and pictures are thus obtained with dye in the *arteries arterioles* and larger *veins By this* means partial or complete vascular obstruction can be seen in the carotid or vertebral circulation Care is needed to distinguish spasm from more permanent obstruction

When the circulation is filled displacement of vessels as by tumours cysts or large ventricles can be seen Subdural haematomas prevent the vascular pattern from reaching the inner table of the skull The vessels may show aneurysms and arteriovenous angiomas Vascular tumours show an abnormal vascular pattern such as the blush of the meningioma

Air Encephalography or Ventriculography Air may be introduced into the subarachnoid space by either lumbar or cisternal *puncture with the patient* sitting upright The air rises into the skull frequently filling the cerebral ventricles and always filling the basal cisterns By making burr holes in the skull air can be put directly into the ventricles by a brain needle

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which occurs towards the end of the fit Similarly acute post traumatic headache is associated with vasodilatation and increased cerebral blood flow This must be distinguished from chronic post traumatic headache

An acute rise of blood pressure as in phaeochromocytoma may give a sudden stress in the intracranial arteries and cause headache of a transient nature This is not the same as the headache in chronic hypertension

(b) *Traction* Brain tumours produce headache by traction on vascular structures and not by raising the intracranial pressure The distorting forces are direct by the tumour and adjacent structures and indirect by extensive displacement of the brain by the tumour or associated hydrocephalus Headache occurs in 80 per cent of patients with brain tumours In most patients especially in the early stages the headache may lateralize the tumour or indicate that it is infratentorial. Usually the headache is non throbbing and intermittent and accentuated by straining or jolting It may not interfere with sleep though it is often present on waking and eased by sitting up Other expanding lesions produce headache in the same way

(c) *Due to Traction and Vasodilatation* Post lumbar puncture headache is produced by this mechanism It may be due to removal of large quantities of C.S F or to continued leakage through the hole made by the needle the occurrence of headache however is quite fortuitous but it is less likely to occur with small bore needles

(d) *Inflammatory* This can be produced by foreign substances such as air or blood or by infection giving meningitis The involvement of the lower cranial nerves and the upper cervical roots gives intense sustained contraction of the occipital and upper neck muscles This is responsible for the stiff neck and causes secondary pain in its turn

Extracranial inflammation as in giant cell arteritis gives a localized headache often of great intensity throbbing and persistent. It is felt as a deep ache often of burning quality and associated with local tenderness With local trauma or infection there is acute local pain and tenderness though the associated headache may be quite mild Unfortunately the superficial scar of a head injury may become an area of persistent pain and tenderness long after it has healed

(e) *Due to Muscular Contraction* This contraction may occur secondary to pain elsewhere and may outlast the original pain It may arise from pain produced in and around the face or from mechanical irritation or inflammation of the cervical nerve roots or from emotional tension The discomfort may consist of a feeling of tightness on one or both sides of suboccipital occipital parietal or frontal regions or true aching pain of great intensity in the same areas There may be considerable spasm nodular areas and tender points in the muscles of the neck and movements may be limited This is a very common mechanism for producing the most prolonged and sustained headaches

Infections

INFECTIONS OF THE MENINGES

Acute Purulent Meningitis

Organisms may reach the ventricles or subarachnoid space by way of the blood stream with or without involvement of other organs of the body They may pass by direct extension from a septic focus in the cranial cavity or head and they may enter through compound fractures of the skull which have torn the dura mater either directly or by fracturing through the nasal sinuses or petrous bones where the dura is adherent to the bone They may be introduced into the subarachnoid space from without during lumbar puncture the administration of spinal anaesthetics or myelography or air encephalography Whatever the causative organism the pathology symptoms and course of the disorder are similar and clinically it is usually only possible to make a diagnosis of meningitis the organism being isolated from the cerebro spinal fluid or from a focus of infection The commonest organism is the meningococcus which accounts for approximately 40 per cent of cases The tubercle bacillus accounts for just under 30 per cent the pneumococcus for 10 per cent the streptococcus for 8 per cent and the influenza bacillus for 6 per cent A miscellaneous group of organisms accounts for the remaining cases

Meningococcal Meningitis

This condition occurs constantly in sporadic form and occasionally in epidemic form especially when there are large shifts in the population as in

All the structures outside the skull are pain sensitive These include the muscles of the scalp and suboccipital regions the linings of nasal cavities the external and middle ears the arteries and soft tissues of the scalp the pericranium and the teeth Pain from any of these structures is sharply localized to the area stimulated and then may spread widely either by being referred through a central mechanism or by producing secondary contraction in the muscles around the scalp and neck

The mechanisms by which pain sensitive structures can be stimulated both experimentally and naturally must be considered in more detail

1 *Dilatation of Cranial Arteries* This may be due to relaxation of the wall or to pressure from within

A characteristic of this type of headache is its throbbing nature the throb being synchronous with the pulse A good example of this is seen in the headache produced by an injection of histamine Here the headache is due to intracranial vascular dilatation It is not easy to produce an experimental dilatation of the extracranial arteries but it can sometimes be done by centrifugal force

If an artery has been dilated for long its wall becomes oedematous and the pain loses its throbbing character At the same time the vessel loses its response to constrictor agents such as ergotamine

2 *Traction upon Intracranial Structures* The easiest means of observing this even in the normal is by sudden and vigorous head movement It can be induced with undue ease and in excessive intensity when the intracranial anchoring vessels are inflamed dilated or displaced This is seen in cerebral tumours The pain in these states is increased by coughing or straining which raise the C S F pressure and so increase the traction

3 *Traction on and Dilatation of Intracranial Vessels* This occurs when 20 ml or more C S F is removed in the upright position producing a moderate or severe headache The headache can be made better by putting fluid back in the lumbar theca or by placing the subject horizontally Removal of C S F produces a swelling of the brain and intra cranial vasodilatation in addition to movement of the brain with resultant traction

4 *Inflammation of Intracranial Structures* This can be shown in a mild fashion by intrathecal injection of air which produces a pleocytosis and acts like an inflammatory condition Pain is felt from almost all the intracranial pain sensitive structures

5 *Contraction of Skeletal Muscles of Head and Neck* It is associated with tightness or pulling feeling and gives a deep steady ache and is aggravated by any movement of the affected muscles The latter often stand out quite prominently

6 *Overflow Headaches as in Reflex Vasodilatation Produced by a Painful Stimulus such as a Toothache* The best experimental study is carried out by reproducing the ice cream headache Certain individuals develop intense frontal head pain when very cold substances touch the roof of the mouth It develops at once and lasts during the time of chilling In all referred headache the degree of localization and spread depends on the intensity and duration of stimulation Pain from the eyes nose or paranasal sinuses or teeth is usually felt in the trigeminal region From the ear it may be felt anteriorly or posteriorly From the upper neck muscles the pain may radiate well forward even to the eyes and cheeks The diagnostic test is the disappearance of pain if the afferent path from the site of impulses is blocked

Clinical Types of Headache

(*a*) *Vascular* This type of headache is best seen in migraine which is described on page 457 and will not be further discussed here

It can also occur in systemic infections as in influenza typhoid typhus or malaria It is distinct from meningitis It is a dull deep ache usually generalized and due to dilatation of intracerebral arteries but in some individuals may also be due to dilatation of extracerebral vessels The intensity of the pain is usually proportional to the fever

Some patients have a dull headache for a short time with the therapeutic use of nitrites This is usually accompanied by facial flushing Tolerance may develop with prolonged use

Prolonged anoxia is associated with cerebral vasodilatation and will give an intense headache This is familiar at high altitudes before adaptation occurs Hunger may produce a headache particularly in individuals who are prone to vascular headache When fully developed it may persist even after ingestion of food The response of this headache to jolting straining and lowering of arterial pressure suggests it is due to vascular dilatation but the mechanism is obscure

Hangover headache has all the characteristics of a vascular dilatation The headache however usually develops some time after the blood alcohol level has fallen from its maximum While alcohol is a potent vasodilator it seems as though its effect here is indirect and associated with the loss of sleep exhaustion and emotional stresses that are associated with heavy drinking The alleged association of the hangover with impurities in alcoholic drinks is not proven

The post epileptic headache lasts for several hours after a fit and is due to the profound vasodilatation

continued for 4 to 7 days after complete sympto matic recovery Intrathecal injections of sulphona mide should never be used After the initial lumbar puncture a further examination of the cerebro spinal fluid should be made in 24 hr and subse quently at 48 hr intervals to follow the course of the infection During the administration of sul phonamides ample fluids at least 2 l daily for an adult must be given to prevent urinary blockage by crystallization and it is helpful to keep the urine alkaline thus increasing the solubility of the drug If there has been no response to sulphadiazine in 24 hr the patient should be given 1 mega unit of penicillin 2 hourly

Pneumococcal Meningitis

This infection is rarely primary it is usually a complication of infection of the nasal sinuses middle ear or lung or of fractures of the skull

The symptoms physical signs and investigation findings are the same as those of other forms of acute purulent meningitis The diagnosis can be made without difficulty from the large number of organisms in the cerebro spinal fluid Before the introduction of sulphonamides the mortality rate was almost 100 per cent at present it is between 50 and 60 per cent In view of the high mortality blunderbus therapy is advisable Sulphadiazine is given as described above in the treatment of menin gococcal meningitis along with 1 million units of penicillin every 2 hr intramuscularly In addition a wide spectrum antibiotic such as oxytetracycline may be given intravenously in an initial dose of 500 mg followed by 250 mg every 4 to 6 hr until the patient can take the drug orally Infants are given approximately one half the adult dose Treat ment should be continued for at least two weeks and if there is a constant bacteraemia for much longer It should never be stopped until at least a week after the patient is symptom free and the cerebro spinal fluid is normal When the infection has followed a fracture of the skull entering one of the nasal sinuses there may be a persistent cerebro spinal fluid fistula The dura should then be closed by a plastic operation as otherwise the meningitis will almost certainly recur perhaps weeks months and occasionally even years later

Staphylococcal Meningitis

This is relatively rare and is usually due to spread from skin infections not infrequently associated with dural sinus thrombosis Treatment is by an antibiotic to which the particular staphylococcus is sensitive

Streptococcal Meningitis

This accounts for approximately 8 per cent of all cases and is always secondary to a septic focus most commonly in the paranasal sinuses Treat ment is similar to that of pneumococcal meningitis together with eradication of the primary focus by surgery if necessary

Influenzal Meningitis

Predominantly a disease of infancy and early childhood Over 50 per cent of cases occur before the age of 2 and 90 per cent before the age of 5 It is more prevalent in the winter months and may be primary or secondary to acute sinusitis or frac ture of the skull. The symptoms and signs are similar to those of the other forms of meningitis The disease usually lasts 10 to 20 days though it may be protracted for weeks or months and rarely it is fulminating Again the diagnosis is made by finding a purulent cerebro spinal fluid under in creased pressure and culturing the organism which can usually be done without difficulty It may also be cultured from the blood fairly frequently in the early stages

The mortality rate in untreated infants is over 90 per cent though in adults spontaneous recovery is more frequent Treatment has reduced the mor tality rate to less than 20 per cent.

The most effective drug is chloramphenicol. The initial oral dose is 50 mg/kg of body weight and this is followed by 30 mg/kg 8 hourly until the patient is free from symptoms and from the organ ism Alternatively sulphadiazine can be given with streptomycin in a dose of 20 mg/kg intra muscularly every 12 hr Fifty to 100 mg of strepto mycin may also be given intrathecally daily though it is uncertain whether this is useful

Tuberculous Meningitis

This is always secondary to tuberculosis elsewhere in the body Most commonly the focus of infection is the lungs but it may be in lymph glands bones nasal sinuses or any other organ The onset of meningeal symptoms may coincide with the de velopment of acute miliary dissemination or with increased activity of the primary focus Occasionally the meningitis is the only manifestation of activity The meningitis is probably secondary to the rupture of a caseous focus in the brain in contact with the subarachnoid space or the ventricles this focus having been produced via the blood stream from the primary tuberculous lesion elsewhere Occa sionally bacilli lodge directly in the meninges or choroid plexus after an acute miliary dissemina tion from other viscera In about one quarter of

war or when large bodies of people are living together as in military camps

The disease is spread by droplet infection mainly by carriers who have usually been in contact with a patient and subsequently harbour the meningococcus in the nasopharynx for two or three weeks Carriers are not necessarily immune and after some weeks may develop clinical manifestations of meningitis the meningococci gaining access to the meninges directly from the nasopharynx through the cribriform plate or indirectly by way of the blood stream A meningococcal septicaemia often occurs before the meninges are infected and in some early cases the ventricular fluid may be teeming with organisms before the meninges are infected Not all cases of meningococcal septicaemia go on to meningitis particularly in these days of effective therapy In fulminating cases death may occur before there are any pathological changes in the nervous system but when death does not occur for several days an intense inflammatory reaction of the meninges is found This is especially marked in the sub arachnoid spaces over the convexity of brain over the spinal cord and around the cisterns at the base of the brain It may also extend a short distance along the perivascular spaces into the substance of the brain and spinal cord and occasionally into the parenchyma Meningococci both intra and extra cellularly are found in the meninges and the fluid from the ventricles and sub arachnoid space As the infection progresses the pia arachnoid becomes thickened and adhesions may form anywhere which at the base may interfere with the flow of cerebro spinal fluid thus producing an internal hydrocephalus The inflammatory reaction and subsequent fibrosis may be the cause of the cranial nerve palsies which are occasionally found though these may also be due to involvement of the nutrient arteries With efficient treatment the whole inflammatory reaction settles down and nothing may be found in autopsies carried out later

Clinical Picture The onset is similar in all forms of meningitis It is accompanied by rigors and fever severe headache nausea and vomiting pain in the back stiffness in the neck and prostration Conjunctivitis and herpes simplex are common and a petechial skin rash frequently occurs and is usually evidence of a septicaemia The patient is irritable and later confused and stupor or coma may develop Convulsions are not uncommon particularly in the younger patients Focal neurological signs are rare The temperature is usually between 101 to 103 F but may be normal or even subnormal particularly in elderly patients There is tachycardia and an increased respiratory rate The blood pressure is low only in the acute fulminating cases considered later There is rigidity of the neck perhaps with head retraction and diminution of straight leg raising (Kernig s sign) The reflexes are rarely affected The fundi are normal except occasionally late in the disease when papilloedema may develop

Investigations There is a profound leucocytosis up to 30 000 leucocytes per mm^3 The meningococci can usually be cultured from the blood in over 50 per cent of the early cases and from the skin lesions and the nasopharynx The cerebro spinal fluid is under raised pressure is cloudy or purulent and contains from 2 000 to 10 000 polymorphonuclear leucocytes per mm^3 The protein content is raised and the sugar content is decreased to between 5 and 30 mg per 100 ml The chloride content is moderately or greatly reduced Organisms can be seen *both intra and extracellularly when* specially stained and can be cultured in over 90 per cent of cases

Complications With modern methods of treatment complications are unusual and usually transient The commonest is a palsy of one or other of the cranial nerves but a permanent palsy is rare Permanent deafness due to 8th nerve palsy occurs in approximately 1 to 2 per cent Focal neurological signs such as hemiplegia or monoplegia occur in approximately 1 per cent and are usually transient. A dramatic though extremely rare complication is adrenal haemorrhage (Waterhouse Friderichsen s syndrome) This is most commonly associated with meningococcal septicaemia and is characterized by severe prostration hypotension coma and wide spread petechial haemorrhages in the skin which may coalesce The course is rapid with death usually within 24 hr (*see* p 129)

Diagnosis The diagnosis can be made with certainty only if the organism is isolated from the cerebro spinal fluid but it can be suspected from headache and vomiting fever stiffness of the neck and a petechial cutaneous rash

Prognosis The mortality rate of the untreated condition is between 50 and 90 per cent If the diagnosis is made early and appropriate chemo therapy is given the outlook is now very good except in infants and elderly debilitated individuals and those in whom treatment is started very late

Treatment Sulphonamides give excellent results Sulphadiazine is probably the best because of its high concentration in the cerebro spinal fluid The initial oral or intravenous dose should be 0 05 to 0 1 g/kg of body weight If the patient cannot swallow or is vomiting he should then be given half this amount as sodium sulphadiazine intravenously every 8 hr The subsequent oral dose is 1 to 2 g according to weight every 4 hr This should be

continued for 4 to 7 days after complete symptomatic recovery Intrathecal injections of sulphonamide should never be used After the initial lumbar puncture a further examination of the cerebro spinal fluid should be made in 24 hr and subsequently at 48 hr intervals to follow the course of the infection During the administration of sulphonamides ample fluids at least 2 l daily for an adult must be given to prevent urinary blockage by crystallization and it is helpful to keep the urine alkaline thus increasing the solubility of the drug If there has been no response to sulphadiazine in 24 hr the patient should be given 1 mega unit of penicillin 2 hourly

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all cases the infection is with the bovine bacillus and the remainder with the human bacillus

Pathology The brain is pale and the convolutions flattened and a yellowish gelatinous exudate is found matting the leptomeninges at the base and extending along the Sylvian fissure Military tubercles are present on the leptomeninges and are most easily seen along the vessels especially the middle cerebral artery The parenchyma of the brain shows little inflammatory reaction but marked toxic degeneration of neurones may be present In patients kept alive for months by strepto mycin the basal exudate becomes intensely hard and the large arteries passing through it may de velop an arteritis and produce infarction of the brain Hydrocephalus may also develop if there is an obstruction to the flow of cerebro spinal fluid

Clinical Picture The onset is insidious or sub acute There is almost always an initial phase of vague ill health with lassitude anorexia loss of weight and change of disposition After two or three weeks meningeal irritation may develop with stiffness of the neck and vomiting Convulsions are quite frequent in children in the early stages Head ache becomes progressively more severe and in infants the fontanelles may bulge As the disease progresses the patient becomes stuporose or coma tose and symptoms and signs of damage to the cranial nerves appear together with other focal neurological symptoms The drowsiness stupor and delirium frequently alternate with lucid intervals even in quite late stages of the disease

Examination in the early stages reveals the find ings of meningeal irritation i e fever irritability stiffness of the neck and Kernig s sign The reflexes may be either exaggerated or depressed Signs of raised intra-cranial pressure and focal damage to the nervous system are rarely present at the onset In the later stages papilloedema which may be transient cranial nerve palsies and focal neuro logical signs are common

Diagnosis The certain diagnosis of tuberculous meningitis can be made only by culture of the organisms from the cerebro spinal fluid or by the result of inoculation of this fluid in guinea pigs The cerebro spinal fluid is under increased pressure and has a slightly cloudy appearance with forma tion of a clot on standing and a moderate pleocytosis of from 25 to 500 cells per mm^3 with lym phocytes predominating The protein content is increased to about 100 mg/100 ml The chloride content is reduced to approximately 500 mg/100 ml and the glucose content to below 50 mg/100 ml Although tubercle bacilli can often be found in the fluid their absence is not significant If the cerebro spinal fluid shows these changes it is probably wise to treat the patient as though he is suffering from tuberculous meningitis while awaiting the result of culture or guinea pig inoculation

Prognosis and Treatment. In an untreated case death usually occurs within 3 weeks of the onset of symptoms With modern treatment many cases can be completely cured provided the treatment is insti tuted early and continued long enough. If the patient is comatose when first seen the outlook is usually hopeless The recovery rate varies between 50 and 60 per cent although there may be consider able residual manifestations either as a result of the disease or of treatment

Initially 2 to 3 g of streptomycin should be given daily intramuscularly for an adult, together with isoniazid 3 to 5 mg/kg of body weight daily in divided doses Intrathecal streptomycin used to be given widely and is still given sometimes but there is no proof that patients who have it do better than those who have only intramuscular streptomycin Moreover the daily lumbar punctures are distress ing for the patient and intrathecal streptomycin causes pleocytosis a raised protein content in the cerebro spinal fluid and a tendency to adhesion formation After about 2 weeks the dose of strepto mycin should be reduced to not more than 1 g daily to avoid toxic effects Para amino salicylic acid may be used as an alternative to isoniazid and in gravely ill cases it may be justifiable to use all three drugs simultaneously Cortisone is some times given in the hope of hindering the develop ment of adhesions and blocks If hydrocephalus develops as the result of a spinal block ventricular tapping through burr holes will be needed

The duration of treatment is as yet unsettled Certainly many months of treatment at least are required with the state of the cerebro spinal fluid as a guide The main index of a good response is the disappearance of tubercle bacilli from the cerebro spinal fluid This may occur in the first fortnight in favourable cases though patients have recovered when the organisms have been present intermittently for several weeks The glucose level in the cerebro spinal fluid is probably a more useful index of progress than the chloride level A return of fever and vomiting an increase in headache and irritability and apathy in a patient who has pre viously made good progress are the chief symptoms of relapse while the cerebro spinal fluid will show a fall in glucose content a rising cell count and the reappearance of organisms in films or cultures This calls for a resumption of treatment if it has been stopped Fortunately the development of re sistance to streptomycin by the organism is rare provided it is always given with isoniazid or para amino salicylic acid

Streptomycin often causes toxic effects (*see* p 38) of which deafness can be permanent and vertigo prolonged

After an illness of such severity and length convalescence should be prolonged and a spell in a sanatorium may be desirable After treatment has been stopped a lumbar puncture should be carried out once a fortnight for three months and once a month after this until the fluid is completely normal on two successive occasions

Aseptic Meningitis

This term is used to describe the condition in which there is meningeal irritation and a reaction in the cerebro spinal fluid in the absence of an infecting organism It may be produced by an irritant in the cerebro spinal fluid introduced from without or by disease as when there is an area of necrosis

The physical signs may be very suspicious of actual infection of the meninges as there may be fever headache stiffness of the neck and a positive Kernig s sign The cerebro spinal fluid however has a normal sugar content and no organisms can be found but there is often a pleocytosis and a raised protein content

This condition rarely persists for more than a few days unless actual necrotic tissue is in contact with the arachnoid or ependyma when it may go on until this primary lesion is cleared up

Meningism

In children or young adults there may be headache stiffness of the neck Kernig s sign and occasionally delirium in association with any acute infection These may all suggest acute meningitis or pre paralytic poliomyelitis but the cerebro spinal fluid is normal which excludes meningitis and makes poliomyelitis unlikely The meningeal signs are probably due to a disturbance in the osmotic relationship between the blood and the cerebro spinal fluid with retention of fluid in the body and a more rapid formation of cerebro spinal fluid with a rise of intracranial pressure This is a transient state and clears up fairly soon with disappearance of the symptoms The lumbar puncture which is performed as a diagnostic measure usually relieves the patient completely

SUBDURAL AND EPIDURAL INFECTIONS

Cerebral Subdural Empyema

This is a collection of pus between the dura and the arachnoid of the cranial cavity It may result from direct extension from infections of the nasal sinuses middle ear or meninges as a complication of compound fracture of the skull or from septicaemia It may be caused by any of the pyogenic bacteria The pathological findings depend on the mode of entry of the infection In traumatic cases there may be osteomyelitis of the overlying skull but this may also be found in infections of the sinuses with a spreading venous thrombosis Free pus or granulations may be present on the outer surface of the dura The purulent exudate in the subdural space is not encapsulated There may be some softening of the cortex beneath the most heavily infected regions

Clinical Picture There may be local pain and tenderness from the primary focus Rigors fever and severe headache are common initial symptoms and there may be neck stiffness and a positive Kernig s sign Confusion somnolence or coma may develop later Thrombophlebitis of the cortical veins is associated with focal or generalized convulsions and focal neurological signs

Investigations There is a leucocytosis in the blood X rays of the skull may show evidence of infection or osteomyelitis The cerebro spinal fluid is sterile under increased pressure and shows a moderate pleocytosis only with varying cells The protein content is usually raised and the sugar content is normal

The diagnosis is not easy but should be suspected in a patient with a primary infected focus in the skull associated with headache and stiffness of the neck The mortality rate is high partly because of failure to make the diagnosis Prompt evacuation of the pus and treatment with antibiotics may lead to recovery even after focal neurological signs have appeared The subdural space however is particularly difficult to drain effectively

Spinal Epidural Abscess

Though not a common condition this is most important because early diagnosis and effective treatment can save the patient from a complete and permanent paraplegia The abscess may be acute or a chronic purulent granuloma Infection may reach the epidural space as a direct extension from inflammatory processes in adjacent tissues perforating wounds or lumbar puncture and by the blood stream from infections elsewhere in the body which is probably the most common cause An osteomyelitis of the lamina frequently precedes the epidural infection The primary site of infection is often the skin but may be in the tonsils uterus

or elsewhere Occasionally minor trauma is the immediate preceding cause The common organism is the *Staphylococcus aureus* but others have been described The condition may occur anywhere in the spine but most often in the mid dorsal region

The lesion in the spinal cord depends on the extent to which the infection has progressed before treatment is started Necrosis of the periphery of the cord may result from pressure of the abscess or myelomalacia of one or several segments may occur when the veins or arteries are thrombosed There is degeneration on either side of the necrotic lesion Very rarely the infection extends into the spinal cord itself with abscess formation

Clinical Picture The preceding infection may be so slight as to be overlooked Severe pain in the back or legs comes on quite suddenly and is followed within hours or days by stiffness of the neck headache malaise and fever Later rapidly ascending paralysis of the lower extremities with sensory loss and sphincter paralysis develop Acute girdle pains may mark the upper margin

Investigations Occasionally a needle inserted into the epidural space aspirates pus if not the evidence of a block in the cerebro spinal fluid may be found with xanthochromia a moderate pleo ytosis and a great rise in protein content

Prognosis and Treatment The abscess should be drained by laminectomy as a matter of urgency and anti bacterial drugs given Following this rehabilitation of the patient to make the best use of the returning function in the lower limbs is needed The amount of return of function depends on the degree of damage to the spinal cord and this in turn depends on the duration of the condition before treatment

INFECTIONS OF THE INTRACRANIAL VENOUS CHANNELS

The large dural sinuses may become thrombosed when they are infected or when there is neighbourhood infection in the epidural or subdural spaces Sinus thrombosis also occurs in severely dehydrated or marasmic infants and in the subjects of blood dyscrasias particularly polycythaemia and leukaemia In addition the sinuses may be occluded by trauma or tumour masses The small cerebral veins are usually only affected as an extension of the thrombotic process from the larger dural sinuses More rarely they are the site of a primary infection Occlusion of the cortical and the subcortical veins causes focal neurological symptoms and signs The most frequently thrombosed sinuses are the lateral cavernous and superior sagittal

Lateral Sinus

Thrombosis of the lateral sinus is usually secondary to middle ear infection and mastoiditis Its incidence has greatly decreased since the introduction of the anti bacterial drugs and it is now rare It may be accompanied by septicaemia particularly if the infection is due to the haemolytic streptococcus and the signs and symptoms of the septicaemia may be superimposed upon and overwhelm those due to the sinus thrombosis

Clinical Picture Lateral sinus thrombosis causes fever and rigors and also headache nausea and vomiting which may be due to an increase of the intracranial pressure This occurs more frequently when the right sinus is obstructed because this drains the greater part of blood from the brain Sometimes distension of the superficial veins in the neck and tenderness over the course of the jugular vein in the neck may be found Papilloedema usually bilateral develops in about half the cases because of this raised intracranial pressure Unilateral papilloedema usually means that the process has extended to one of the cavernous sinuses Drowsiness and coma may occur but convulsions are infrequent and focal symptoms are rare Occasionally a hemiplegia occurs due to spread of thrombosis into the cortical veins of one hemisphere but this should raise suspicions of a cerebral hemisphere abscess Diplopia due to an external rectus palsy is sometimes present but usually means that the inflammation has involved the tip of the petrous bone causing paresis of the abducens nerve and irritation of the trigeminal nerve with consequent pain in the face (Gradenigo s syndrome) More rarely the syndrome of a lesion in the jugular foramen is present This is a paresis of the 9th 10th and 11th nerves and is thought to be due to pressure from a distended jugular vein or to extension of the infection into the bone around the foramen

Investigations There is a leucocytosis and often a positive blood culture The cerebro spinal fluid shows changes of an aseptic meningeal reaction with an increase in pressure The fluid is turbid and contains many leucocytes but the sugar and chloride content are normal and cultures are sterile

Diagnosis and Treatment The only important differential diagnosis is from an intracerebral abscess Focal signs such as hemiplegia aphasia or hemianopia are very suggestive of an abscess and this must always be excluded by full investigation

Sinus thrombosis carries a high mortality if untreated The most important part of treatment is

prophylaxis by the use of anti bacterial drugs in preceding infections The actual lateral sinus thrombosis should be treated by anti bacterial drugs surgical drainage and ligation of the jugular vein if there is any possibility of a pyaemia Those cases which recover may show a raised intracranial pressure for many months due to the occlusion of the jugular vein

Cavernous Sinus

Cavernous sinus thrombosis is usually secondary to suppuration in the orbit nasal sinuses or the face While one sinus is usually affected at first the infection rapidly spreads through the circular sinus to the opposite side Non suppurative thrombosis is rare though it may be associated with a total or partial occlusion of the sinus by tumours trauma or aneurysms

This is an extremely acute condition The patient is very ill with a septic type of fever There is pain in the orbit which is also painful to pressure and the eye is proptosed with considerable oedema and chemosis of the conjunctiva and eyelid Diplopia is frequent as a result of unequal protrusion of the eyes and involvement of the external ocular nerves and ptosis may be present. The optic discs are swollen and when the orbital veins are obstructed are surrounded by numerous haemorrhages The cornea may be cloudy and even ulcerate The pupil may be of any size The pupillary reactions and visual acuity are variable

Blood and cerebro spinal fluid findings are exactly the same as in lateral sinus thrombosis and the diagnosis should not be difficult Other causes of exophthalmos and congestion in the orbit must be excluded though none are associated with a septic temperature and such profound illness Arterio venous aneurysm is differentiated by the bruit and by the pulsating exophthalmos which can be abolished by occlusion of the carotid artery

The treatment is with anti bacterial drugs before their introduction the condition was invariably fatal

Superior Sagittal Sinus

Thrombosis of this sinus is less commonly infective than that affecting the lateral and cavernous sinuses though infection may cause it by extending from the nasal cavities or from other infected sinuses It may also be thrombosed as the result of osteomyelitis of the skull and it is the common site of non septic thrombosis in infancy

The signs of infective thrombosis are much the same as those of infective thrombosis of the other large venous sinuses *i e* prostration fever and raised intracranial pressure There may also be local signs of oedema of the forehead and anterior part of the scalp and engorgement of the veins around the anterior and posterior fontanelles even with the formation of a caput medusae If the clot extends into the larger cerebral veins there is frequently a hemiplegia and there may be aphasia hemianopia or convulsive seizures

The cerebro spinal fluid and blood findings are much the same as those of thrombosis of the other large sinuses The diagnosis should be considered in everyone with a septic focus in the head when there are convulsive seizures and focal neurological signs It should be particularly considered in infants who develop raised intracranial pressure and cerebral symptoms during the course of any severe nutritional disturbance

The outlook is poor even with anti bacterial drugs Surgical evacuation of the clot from the sinus may be considered when the conservative measures appear to be failing

Otitic or Toxic Hydrocephalus

Following otitis media and infections of the cranial air sinuses and other parts of the respiratory tract and less commonly following infections elsewhere and minor head injuries some patients develop raised intracranial pressure with papilloedema moderate headache and occasionally vomiting Focal neurological signs are either absent or extremely slight Because the first cases described followed otitis media the condition is usually given the name otitic hydrocephalus though benign intracranial hypertension has been suggested as an alternative The raised intracranial pressure is thought to be due to thrombosis of a major lateral sinus or the superior longitudinal sinus The condition is benign usually clearing up without sequelae in from 6–15 weeks

A similar benign condition with a short course occurs in women usually in the fourth decade following pregnancy or miscarriage or associated with obesity The cause of the raised intracranial pressure is unknown though it has been suggested that it is due to an alteration in the electrolyte balance secondary to endocrine disturbance

In mild cases no treatment is needed When the intracranial pressure is persistently very high repeated lumbar puncture should be done and fluid drained off till the pressure falls to about 150 mm otherwise there may be progressive visual loss secondary to the papilloedema

Brain Abscess

Brain abscesses may be of any size from microscopic collections to those involving the greater part of the hemisphere They may arise from direct extension from infection within the cranial cavity

(*particularly in the nasal sinuses* middle ear and mastoid) from osteomyelitis of the skull or infection due to fracture or from metastatic spread of infection elsewhere in the body

Metastatic abscesses are usually secondary to suppuration in the lungs such as bronchiectasis or lung abscess They may also be associated with a bacterial endocarditis which is often superimposed on congenital heart disease or from septic foci in the throat and upper respiratory pathway

Intracerebral abscesses are usually single but may be multilocular less commonly they are multiple During its development the abscess passes through three stages The first is an acute encephalitis without visible pus formation In the second stage pus is present but the abscess is not well defined In the third stage a definite capsule is formed and the abscess is then localized

Clinical Picture The symptoms of brain abscess are much the same as those of other expanding brain lesions Symptoms of infection except those due to the primary focus may be lacking As there is considerable oedema of the brain around the developing abscess raised intracranial pressure develops very rapidly and headache nausea and vomiting are early symptoms Focal or generalized convulsions are common The temperature may not be elevated unless due to the primary cause The pulse and respiratory rate are dependent upon the intracranial pressure Some degree of swelling of the optic discs is present in about half the cases but this depends greatly upon the site of the abscess False localizing signs due to pressure on the ocular motor nerves or brain stem may be present Focal signs develop according to the site of the abscess There may be hemiparesis or hemiplegia with mental confusion and apathy particularly if the abscess is anteriorly placed Temporal or parieto occipital involvement may be accompanied by hemianopia and aphasia and cerebellar involvement by ataxia intention tremor nystagmus and hypotonia Frequently the signs are quite slight

Investigations The cerebro spinal fluid varies according to the degree of localization of the abscess When it is well localized the fluid is clear with some rise of pressure There is usually a pleocytosis of less than 100 cells/mm^3 the majority of which are leucocytes The protein is usually raised out of all proportion to the cell content There is no diminution of the chloride or sugar content Organisms are absent The cerebro spinal fluid is that of frank purulent meningitis if the abscess ruptures into the ventricles or subarachnoid space

The electroencephalogram may give valuable evidence as to the site of an abscess as the oedema around it causes great changes which may be diagnostic Ventriculography may be needed for complete localization of the abscess but this should usually be performed just before a surgical attack on the abscess is to be carried out

Diagnosis and Treatment The main differential diagnosis is from other space occupying lesions in the brain Abscess is rare without an evident source of infection though occasionally the primary cause of a chronic abscess may have completely disappeared and may not be suspected The diagnosis then is very difficult and is often not made until the lesion is exposed at operation

The outlook in an untreated brain abscess is with rare exceptions fatal

The treatment of brain abscess is surgical evacuation of the pus with excision of the capsule if this can be done with safety Operation used to be delayed until the abscess was firmly encapsulated but anti bacterial drugs now make possible an earlier attack before a firm capsule is present The abscess may have to be drained by repeated puncture through a skull opening and to assist this the abscess cavity may be filled with radio opaque material which enables its size and situation to be determined with certainty by X ray

The sequelae of a brain abscess are residual focal neurological defects Prophylaxis with anti-convulsants should probably be given to all patients for a year or even two after the abscess is regarded as healed

VIRUS DISEASES OF THE NERVOUS SYSTEM

The neurotropic viruses are those which attack the nervous system primarily They include the viruses of rabies anterior poliomyelitis and various forms of equine encephalitis and lymphocytic choriomeningitis Encephalitis lethargica inclusion encephalitis and herpes zoster have never been transmitted to animals but are also thought to be due to neurotropic viruses Other viruses which are not normally neurotropic sometimes attack the nervous system the best examples are mumps and infectious mononucleosis

The viruses are obligatory intracellular parasites and damage the nervous system by directly attacking the ganglion cells Their greatest affinity is for the grey matter and they may cause any degree of damage up to complete necrosis

Poliomyelitis

Poliomyelitis is an acute virus infection of the central nervous system in which the grey matter of the brain and spinal cord is almost exclusively affected The virus which is one of the smallest known has three immunologically distinct types type 1 (Brunhilde) type 2 (Lansing) and type 3 (Leon) Each of these types can again be subdivided into various strains Not very much is known at present about the prevalent types and strains that are chiefly responsible for the disease as we see it in Britain to day but it is thought that a change in incidence has taken place during the last 25 years because the disease itself has altered in certain important epidemiological characteristics Previously as the old name of infantile paralysis indicates poliomyelitis was a sporadic illness affecting in the main young children multiple cases in a family were rare paralysis chiefly affected spinal muscles and involvement of the brain stem was unusual Now although cases of this kind are still common the disease tends to be more epidemic in nature adolescents and young adults are more often attacked contact infection is more common and brain stem involvement is alarmingly frequent These are on the whole the characteristics of a type 1 virus infection and it seems not unlikely that the reason for the change in the character of the disease is that type 1 infection previously unusual has now become much more common in this country

Man and the chimpanzee seem to be the only animals naturally susceptible to poliomyelitis although other kinds of monkey can be experimentally infected There has been much argument as to the method of entry of the virus but the pharynx and the alimentary tract are probably the chief portals The virus from infected droplets in the pharynx may travel along the lower cranial nerves to reach the brain stem and the virus in food and drink may invade the spinal cord by migrating from the alimentary tract along the sympathetic nerves In either case there is usually at one time or another a transient virus invasion of the blood stream The virus is present in the faeces of poliomyelitis patients and carriers and flies are thought to be possible vectors of infection from sewage to food However in most cases of ingestion infection faecally contaminated hands are probably the means whereby the food is infected

Poliomyelitis is rare in early infancy and after the age of 45 Second attacks are very unusual but are not unknown No race or social class is immune but the disease is more common in civilized communities and frequently attacks healthy cleanly well nourished individuals The reason for this disconcerting preference is not clear but it is curious that whereas bacteria tend on the whole to attack poorly nourished debilitated people and to spare those in vigorous health viruses sometimes seem to do just the opposite Poliomyelitis can appear sporadically at any time of the year but is most prevalent during the summer and autumn months In recent years epidemics have tended to appear in Britain between July and November During epidemics the ratio of subclinical to clinical infection is high In all probability most people are infected by the virus at one time or another but few show any symptoms and only a very small proportion develop paralysis It is important to bear this in mind for two reasons the large number of symptomless cases explains why it is so difficult to check the spread of an epidemic and a realization of the relatively small number of people that develop serious paralytic disease enables one to keep a sense of proportion about poliomyelitis The disease has now displaced tuberculosis in the mind of the general public as the infection most to be feared and during an epidemic public alarm is often unreasonably great

The virus primarily attacks nerve cells though the interstitial nerve tissues and the meninges are also affected to some extent Lesions can be found in the cerebrum thalamus and cerebellum but the brunt of the attack is borne by the motor cells of the medulla and spinal cord and the major manifestations of poliomyelitis result from destruction of these cells Clinical paralysis only follows when at least 90 per cent of the anterior horn cells of a particular spinal segment are destroyed Nevertheless although lower motor neurone damage is the dominant feature of severe clinical poliomyelitis an encephalitis of some degree is present in nearly every case Non paralytic illnesses with encephalitic features are common during poliomyelitis epidemics and are almost certainly caused by the same virus

Clinical Picture The incubation period is very variable but is usually about 12 days

The clinical course of the disease is also variable As already noted the virus first invades the upper respiratory or alimentary tracts then the blood stream and finally may attack the central nervous system but its progress may be halted by the bodily defences in any one of these situations If the infection remains localized to the pharynx or to the alimentary canal no symptoms develop the infection is subclinical If it invades the blood stream a mild febrile illness results often with a sore throat and generalized glandular enlargement and sometimes with vomiting and diarrhoea This upset which lasts only a few days is often termed the

minor illness of poliomyelitis The infection may stop here but in some cases it goes on to produce after a latent period of 3 or 4 days the so called major illness The temperature rises again and now there are signs of meningeal irritation headache backache some neck stiffness and a positive Kernig s sign The patient looks flushed and apprehensive and is easily fatigued In non paralytic cases this is all that happens after a few days the temperature falls and all is well The motor neurones of such patients are almost certainly damaged but not enough to produce clinical paralysis

However a few patients continue to be feverish and then develop paralytic manifestations There is at first tenderness fibrillary twitching and pain on stretching the affected muscles and the corresponding tendon reflexes may be exaggerated A few hours or days later flaccid weakness supervenes tenderness goes and the tendon reflex is diminished or lost Sometimes the degree and extent of muscular weakness is maximal at its onset but not infrequently it gradually extends over a *matter of days For* example paresis may first appear in the peroneal muscles of one leg then gradually spread to involve all the muscles of that leg and perhaps some muscles in the other leg or in an arm Occasionally weakness appears in one part and then after a *latent period of several days suddenly appears in* another part In general so long as pyrexia continues there is always a risk that further paralysis *may occur and it is never possible at the outset to* forecast the degree and extent of the ultimate paralysis

Variations on this pattern of illness are very common The minor illness may be absent or so slight that it is unrecognized and the major illness *is then the first obvious manifestation* Paralysis is sometimes the presenting symptom other symptoms having been negligible The disease may be *apyrexial throughout* Sometimes encephalitic symptoms such as severe headache delirium and acute Parkinsonism predominate Poliomyelitis is a protean disease

Course and Complications Pyrexia in the major illness seldom lasts more than a week and when it subsides the patient is convalescent being left with a variable degree of paralysis This may take many months to recover and in some cases permanent weakness remains Unless however a muscle is *completely* paralysed during the acute stage of the illness it is likely to regain almost full power Even if completely paralysed initially it may well recover in time to a useful extent

Life is seldom threatened in poliomyelitis unless the muscles of respiration are involved but when they are the situation is always serious *It is more* serious still when in addition the medullary (bulbar) motor centres are affected for now the patient is neither able to breathe properly nor to swallow and cough Unless *promptly treated* such patients die either from asphyxia or from pulmonary collapse and infection due to the inhalation of pharyngeal secretions *Respiratory muscle weakness* is shown by rapid but shallow breathing inability to hold the breath for more than a few seconds use of the accessory muscles of respiration paradoxical movement of the diaphragm and the eventual development of cyanosis Bulbar involvement *is signalled by an indistinct voice* choking and spluttering when drinking and by the rattling sound of unswallowed pharyngeal secretions as the patient breathes

Signs of damage to the cranial nerve nuclei in the pons and mid brain are unusual but paralysis *of the 5th or 7th nerves can occur* and ocular palsies are sometimes observed Bulbar and cranial nerve palsies in a patient who lives nearly always *recover completely*

Sphincter disturbances are not uncommon but are usually transient and never permanent

Diagnosis *Poliomyelitis is difficult or impossible* to diagnose with certainty before paralysis appears though a prevailing local epidemic may make *suspicion strong During such* an epidemic it is wise to regard any acute febrile illness of which the cause is not clear as probably poliomyelitis *especially if there is* some headache or some such neurological symptom as urinary retention Signs of mild meningeal irritation such as backache neck *stiffness* and an inability to sit up and kiss the knees further increase suspicion The clinical picture at this stage is simply that of a virus meningitis and is by no means diagnostic of poliomyelitis infection However a careful history may elicit the symptoms of a preceding minor illness and there may even on rare occasions be a story of contact with a known case of the disease But in many instances a definite diagnosis will have to await the appearance of muscular weakness There is as a rule no great harm in such delay (for as yet we have no specific treatment for poliomyelitis) provided the suspect is isolated The only real danger is that the illness might in fact be a bacterial meningitis in which case delay in diagnosis and treatment would be unfortunate Such an error should not however normally arise for the patient with bacterial meningitis has a much more intense headache has signs of severe meningeal irritation and looks much more *ill than the patient with pre paralytic polio*myelitis But if there is any doubt, a lumbar puncture should be done at once In acute bacterial *meningitis the cerebro spinal fluid* is often turbid

and under pressure the granulocytes in it are markedly increased in number and the sugar and chlorides are decreased In early poliomyelitis the fluid is clear there is a mild pleocytosis with lymphocytes usually predominating the protein is slightly increased and the sugar and chloride content is normal Tuberculous meningitis should not as a rule cause any diagnostic difficulty it is a slowly-developing disease and there is usually a history of several weeks of preceding ill health

Apart from excluding bacterial meningitis and the occasional case of hysterical pseudo poliomyelitis lumbar puncture does not help much in the diagnosis of poliomyelitis for the findings are the same in any virus infection with meningeal involvement Indeed there are grounds for avoiding it at this early stage as it may possibly aggravate the disease process (*see* below)

When paresis appears the diagnosis is usually clear The only other febrile disease with developing flaccid muscular paralysis that is likely to cause confusion is the rare polyneuritis of Guillain Barré type (*see* p 433) In polyneuritis however the paralysis is symmetrical and there are objective sensory disturbances In poliomyelitis the paralysis is rarely if ever symmetrical and objective sensory loss is not found In the Guillain Barré syndrome the cerebro spinal fluid shows no increase of cells but a markedly raised protein content Rarely muscular weakness with fever is seen in polyarteritis nodosa or in porphyria but there are usually other features which make these diseases recognizable

During poliomyelitis epidemics fear of the disease may produce some cases of hysterical pseudo paralysis These patients unless they have some concomitant illness are apyrexial their tendon reflexes are brisk and their apparent muscular weakness has the usual hysterical features The cerebro spinal fluid is of course normal

It is possible to culture poliomyelitis virus from the stools of patients with the disease and it is also possible to demonstrate neutralizing and complement fixing antibodies in the blood At present these diagnostic methods are technically too difficult and too slow to be of much practical value in bedside diagnosis but it is to be hoped that quicker and simpler techniques will soon be developed The present tests are however epidemiologically useful in tracing the incidence and spread of infection and in studying the behaviour of the different types of virus

Treatment. Suspected cases of poliomyelitis should at once be put to bed and isolated Fatigue and muscular strain in the early stages of the disease undoubtedly increase the risk of severe neurone damage Trauma of any kind should be avoided lumbar puncture should not be done lightly nor should intramuscular injections of antibiotics be given unless absolutely necessary Routine prophylactic inoculations for example against diphtheria should not be given even to apparently healthy children during poliomyelitis epidemics for there is good evidence that even this slight trauma may convert a silent subclinical infection into a paralytic one Similarly routine tonsillectomies should be kept to a minimum during the summer and autumn months and suspended altogether during a poliomyelitis epidemic

Muscular aching in the early stages can be relieved by hot packs and by aspirin Many patients are restless and frightened and need to be quietened and reassured Sedation with oral amylobarbitone 100 mg (1½ gr) or with a tranquillizing drug such as meprobamate 400 mg 3 times daily will help

When paresis has developed the weak muscles should be supported on pillows or light plastic splints Care should be taken not to fatigue the patient by repeated prolonged physical examination in the acute stage detailed assessment of the degree and extent of paralysis can well wait until the temperature has become normal

Extensively paralysed patients need skilled nursing Frequent change of posture are desirable and the bedclothes must be kept scrupulously clean and smooth for the skin of these patients is often extremely sensitive

Opinions differ as to when active reablement of the weak muscles should begin but it seems reasonable to start as soon as the acute phase of the illness is over The exercises should be supervised by an experienced orthopaedic surgeon and treatment will often be necessary for 6 months or even longer The deformities which result from permanent paralysis can be minimized by orthopaedic operations and appliances

During the stage of acute paralysis there is much protein destruction in the affected muscles and a high protein diet during early convalescence is therefore desirable

Respiratory paralysis needs treatment by artificial respiration in some form of breathing machine In Britain the modified Both box respirator (iron lung) is commonly employed It is essentially an oblong metal box in which the patient lies with only his head outside An electrically driven bellows rhythmically lowers the air pressure in the box and this negative pressure forces the patient s thorax to expand The bellows can also if necessary produce positive pressure to assist expiration but as a rule the elastic recoil of the lungs will do this without help

Bulbar paralysis without respiratory paralysis is

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Variations on this pattern of illness are very common The minor illness may be absent or so slight that it is unrecognized and the major illness is then the first obvious manifestation Paralysis is sometimes the presenting symptom other symptoms having been negligible The disease may be apyrexial throughout Sometimes encephalitic symp toms such as severe headache delirium and acute Parkinsonism predominate Poliomyelitis is a protean disease

Course and Complications Pyrexia in the major illness seldom lasts more than a week and when it subsides the patient is convalescent being left with a variable degree of paralysis This may take many months to recover and in some cases per manent weakness remains Unless however a muscle is *completely paralysed during the acute stage of the illness it* is likely to regain almost full power Even if completely paralysed initially it may well recover in time to a useful extent

Life is seldom threatened in poliomyelitis unless the muscles of respiration are involved but when they are the situation is always serious It is more serious still when in *addition the medullary (bulbar)* motor centres are affected for now the patient is neither able to breathe properly nor to swallow and cough Unless promptly treated such patients die either from asphyxia or from pulmonary col lapse and infection due to the inhalation of pharyngeal secretions Respiratory muscle weakness *is shown by rapid but shallow breathing inability* to hold the breath for more than a few seconds use of the accessory muscles of respiration para doxical movement of the diaphragm and the eventual development of cyanosis Bulbar involve ment is signalled by an indistinct voice choking and spluttering when drinking and by the rattling sound *of unswallowed pharyngeal secretions as the patient* breathes

Signs of damage to the cranial nerve nuclei in the pons and mid brain are unusual but paralysis of the 5th or 7th nerves can occur and ocular palsies are sometimes observed Bulbar and cranial nerve palsies in a patient who lives nearly always recover completely

Sphincter disturbances are not uncommon but are usually transient and never permanent

Diagnosis Poliomyelitis is difficult or impossible to diagnose with certainty before paralysis appears though a prevailing local epidemic may make suspicion strong During such an epidemic it is *wise to regard any acute febrile illness of which* the cause is not clear as probably poliomyelitis especially if there is some headache or some such neurological symptom as urinary retention Signs of mild meningeal irritation such as backache neck stiffness and an inability to sit up and kiss the knees further increase suspicion The clinical pic ture at this stage is simply *that of a virus meningitis* and is by no means diagnostic of poliomyelitis in fection However a careful history may elicit the symptoms of a preceding minor illness and there may even on rare occasions be a story of contact with a known case of the disease But in many in stances a definite diagnosis will have to await the *appearance of muscular weakness* There is as a rule no great harm in such delay (for as yet we have no specific treatment for poliomyelitis) provided the suspect is isolated The only real danger is that the illness might in fact be a bacterial *meningitis* in which case delay in diagnosis and treatment would be unfortunate Such an error should not however *normally* arise for the patient with bacterial meningitis has a much more intense headache has signs of severe meningeal irritation and looks much more ill than the patient with pre paralytic polio myelitis *But if there is any doubt* a lumbar puncture should be done at once In acute bacterial meningitis the cerebro spinal fluid is often turbid

Involvement of the Gasserian ganglion occurs in about 5 per cent of patients Any division of the ganglion may be affected but most often the first This is serious because panophthalmitis may follow Occasionally the otic or geniculate ganglion is involved with paralysis of the facial muscles The vesicles may then be confined to the tympanic membrane the external auditory canal or the pillars of the fauces

Rarely a myelitis develops with involvement of the tracts in the spinal cord occasionally producing an incomplete transverse lesion (Brown Sequard syndrome) The cerebro spinal fluid shows a variable lymphocytic pleocytosis with a rise in protein content

The most important complications of herpes zoster are changes in the eyes (as already described) scarring and post herpetic neuralgia The latter occurs most commonly in elderly debilitated patients and may be most obstinate and depressing going on for months or even years and refractory to all treatment

Treatment There is no specific treatment The vesicles should be kept dry and secondary infection prevented If the eyes are involved atropine drops and antiseptic or antibiotic drops in the conjunctiva should be used Systemic antibiotics are unhelpful except in so far as they may prevent secondary infection of the vesicles Pain should be controlled by analgesics If this can be achieved in the acute stage the incidence of post herpetic neuralgia is probably lessened Pituitrin ½ to 1 ml subcutaneously and concentrated liver extract intramuscularly have both been claimed to cut short an attack though there is little convincing evidence to support these claims

Persistent post herpetic pain is extremely troublesome and in severe cases analgesics are almost useless Some patients may become so depressed as to be on the verge of suicide Deep X ray irradiation of the affected ganglia may be effective and should probably always be tried soon after the acute stage is over if the pain is not obviously subsiding When the neuralgia does not respond to analgesics it may respond to sedation with sodium amylobarbitone or other barbiturate perhaps combined with dextro amphetamine to counter the depression Increasing doses of chlorpromazine may also be tried with barbiturates Recently it has been suggested that infiltration of the affected region with xylocaine followed by the repeated application of an electrical vibrator will in time markedly reduce post herpetic neuralgia If all else fails interruption of the spino thalamic pathways in the spinal cord should be considered though even this may not be totally successful particularly if the neuralgia is very chronic

Encephalitis Lethargica

This disease occurred in epidemic form between 1916 and 1927 Cases have occurred subsequently though with increasing rarity and in recent years the acute cases have been remarkably few The cause is uncertain though a filterable virus has been implicated

In the acute epidemics fatal cases showed a diffuse inflammatory reaction in the meninges and around the blood vessels of the brain and spinal cord and acute degenerative changes in the neurones The whole brain was affected but the damage was greatest in the brain stem the basal ganglia and the cerebellum

As the whole of the nervous system can be involved every known neurological sign and symptom has been reported in the acute stages

The disease was of acute or subacute onset with fever headache and lethargy which might alternate with insomnia and delirium or produce a reversal in the sleep-rhythm Cranial nerve palsies were common particularly of the ocular motor group Choreiform athetoid and tic like movements alternating with muscular rigidity and tremors occurred in the acute stages The cerebro spinal fluid was almost always normal except perhaps for a slight elevation of pressure and an occasional mild lymphocytic pleocytosis The reported mortality was between 20 and 25 per cent although this figure was probably too high as many abortive cases were not recognized

The after effects are the most important part of the syndrome Parkinsonism may develop which is similar to idiopathic or involutional Parkinsonism (p 447) In addition behaviour disorders emotional instability obsessional traits and mental defect may occur No treatment affected the acute process only symptomatic treatment is available for the sequelae

Post infectious and Post vaccinal Encephalomyelitis

An acute encephalomyelitis may occur in the course of various infections particularly the acute exanthemata of childhood and may also follow vaccination against smallpox or rabies The symptoms and pathological changes are similar in all these cases regardless of the nature of the acute infection though there may be differences in detail Measles german measles and chicken pox are the most common precursors of encephalomyelitis though the incidence is only about one per thousand cases of measles and probably less in german measles and chicken pox

treated by tilting the bed head down and by constant removal of pharyngeal secretions with a suction catheter Drip feeding with milk is carried out through an indwelling small bore stomach tube When bulbar paralysis is associated with respiratory paralysis there is a danger that inhaled pharyngeal secretions will cause pulmonary collapse and infection The powerful negative suction of the Both box respirator increases this danger and although it can to some extent be countered by tilting the respirator head-down it is safer to use positive pressure artificial respiration for these bulbo respiratory cases In this method a tracheotomy is first carried out and through it a cuffed endotracheal tube is passed When the cuff on the tube is inflated it fits the trachea snugly so that no pharyngeal secretions can get past into the bronchi Rhythmical positive pressure inflation of the lungs through the tube is carried out by means of a small manually or mechanically operated bellows

The treatment of respiratory or bulbo respiratory paralysis is a task of considerable complexity and difficulty and can be carried out successfully only by an experienced team of doctors and nurses in specially equipped hospitals Many lives however have been saved by these measures and it is therefore vital to recognize the first signs of respiratory and bulbar muscle weakness so that the patient can be got to the nearest suitable hospital without delay Every hour counts

Prevention During poliomyelitis epidemics personal cleanliness and the avoidance of crowded places are obvious precautions Destruction of flies may help to prevent spread but as vectors of infection flies are probably not so important in Britain as in warmer climates The question of quarantine for contacts is a controversial one but as a minimum precaution it is wise to advise close contacts such as members of the family to segregate themselves as far as possible for 3 or 4 weeks There is good evidence that if one member of a family has overt poliomyelitis all other non immunes in the family will probably be infected though the infection is often silent The patient himself should be isolated for 3 weeks

Passive immunization with gamma globulin gives good temporary protection but its scope is limited by the restricted amount of material available It should be used however to protect children and young adults in hospital when a poliomyelitis case is admitted accidentally to a general ward and should invariably be given to any such children that have recently undergone tonsillectomy Poliomyelitis developing in a child who has just had his tonsils out is very likely to be of the bulbar paralysis type 500 mg is an adequate protective dose of gamma globulin for an infant but children over 7 years of age need about 1 5 g

Active immunization has recently been introduced into Britain and large scale field experiments are being carried out The present Salk type formaldehyde inactivated vaccines seem to be safe but it is too early to assess their efficiency Experience in North America and in other countries however encourages the hope that poliomyelitis will soon be a preventible disease

Herpes Zoster (Shingles)

This is a common disease which produces inflammatory lesions in the posterior root ganglia The causative virus is closely related to that of varicella since either condition may occur following exposure to the other Herpes zoster may accompany systemic infections and localized lesions of the spine or nerve roots such as acute meningitis syphilis tuberculosis Hodgkin s disease carcinomatous deposits and trauma but all the cases are probably of virus origin the disease or local lesion in the spine or nerve roots merely serving to activate the infection

Although the symptoms may be localized to the distribution of one or two sensory roots the pathological changes are more widespread The affected ganglia of the spinal or cranial nerve roots are swollen and inflamed with a mainly lymphocytic infiltration though some polymorphonuclear cells or plasma cells may be present Some of the ganglion cells become swollen and others degenerate and the inflammatory process extends into the root entry zone of the spinal cord and may also affect the meninges The spinal cord as a whole may be affected or the inflammatory reaction may reach only the motor cells in the anterior horn

Clinical Picture The disease may have a generalized onset with headache and fever but most commonly the initial symptom is a neuralgic pain of varying severity in the distribution of the affected roots In 3 or 4 days the appropriate dermatome is reddened and clusters of vesicles appear in different parts of this area The vesicles which contain clear fluid may be discrete or may coalesce Within 10–14 days they are covered with a scab which eventually desquamates leaving a pigmented scar The scars are ultimately replaced by skin devoid of pigment If the vesicles ulcerate or become infected severe permanent scarring may follow

Occasionally there is impairment of cutaneous sensibility and less frequently muscular weakness in the distribution of the affected root Very rarely there is weakness outside the area involved by the vesicles as when a facial palsy is associated with an upper cervical root zoster There may also be headache neck stiffness or confusion

Involvement of the meninges may be relatively diffuse or limited to the sheath of one cranial nerve In the diffuse condition the onset of symptoms is usually insidious frequently with severe nocturnal headache and sometimes with scalp tenderness Papilloedema may occur Apathy and impairment of intellect are common and aphasia may be present Loss of sphincter control is common When the meninges over the convexities of the hemispheres are involved generalized or focal convulsions occur and there may be weakness and inco ordination of the limbs on one or both sides Basal meningitis may involve the optic chiasm leading to optic atrophy defects of the visual fields and disturbances of the hypothalamus causing obesity or narcolepsy Occasionally hydrocephalus occurs Abnormalities of the pupil responses are almost constant and cranial nerve palsies particularly of the 3rd nerve are common

Any cerebral artery may be involved by a syphilitic endarteritis There may be premonitory motor or sensory symptoms due to ischaemia of the area supplied by the vessel with an eventual thrombosis giving the symptoms of infarction The middle cerebral artery is most frequently affected Hemiplegia of syphilitic origin is rarely associated with loss of consciousness but is often associated with headache Cerebral gummas are extremely rare

Occasionally this form of syphilitic infection is confined entirely to the spinal cord The spinal meninges may be affected by a pachymeningitis commonest in the cervical region and resulting in the so-called pachymeningitis cervicalis hypertrophica This condition however may occur apart from syphilis

Affection of the leptomeninges causes degenerative changes with resultant myelitis of the superficial parts of the spinal cord If the spinal vessels develop an endarteritis the myelitis affects the spinal cord either completely or partially

Usually in these conditions there is pain in the back or neck due to strangulation of the posterior spinal roots and there may be atrophy of muscles supplied by the anterior roots When the cord is involved weakness of the lower limbs develops over the course of a few hours to several weeks A complete flaccid paraplegia may develop quite rapidly with retention of urine and impairment or loss of all forms of sensation below the level of the lesion When the onset is more gradual the functions of the cord are usually less severely affected the para paresis being usually spastic and sometimes accompanied by flexor or extensor spasms

The cerebro spinal fluid contains between 20 and 100 cells mm³ which are almost entirely mono nuclears The protein content of the fluid lies between 50 and 150 mg/100 ml with an increase in globulin The Wassermann reaction is positive in 90 to 100 per cent of cases where the meninges are involved but only perhaps 70 per cent of cases where the vessels alone are involved The Lange colloidal gold test gives a paretic curve (e g 5 542 210 000) or a luetic curve (e g 1 235 542 100)

Treatment Penicillin in large doses is the basis of treatment To diminish the risk of a Herxheimer reaction a preliminary course of mercury and iodide by mouth and bismuth by intramuscular injection twice a week should be given for two or three weeks One million units of penicillin a day should then be given for 15 to 20 days either as one daily injection of a more slowly absorbable compound such as procaine penicillin or as two daily injections of crystalline penicillin The cerebro spinal fluid should be re examined three to six months later when it is hoped that the cell count and protein will have reverted to normal The Wasserman reaction and the colloidal gold curve respond much more slowly and the Wassermann reaction may never become negative If the fluid is very abnormal after three to six months a further course of penicillin should be given and the cerebro spinal fluid again examined up to six months later Treatment with pyrexia as by artificially induced malaria is reserved for patients who fail to respond to penicillin

Effective treatment of neurosyphilis may not result in the complete clearance of all focal lesions These should be treated in the same manner as focal lesions produced by any vascular occlusion (p 411)

Parenchymatous Neurosyphilis (Tabes Dorsalis)

The pathological changes are found in the posterior nerve roots and ganglia in the posterior columns of the spinal cord and in the brain stem The other manifestations of neurosyphilis involving meninges and vessels may be superimposed A combination of tabes and of parenchymatous degeneration of the brain (general paralysis of the insane or dementia paralytica) is not uncommon

Clinical Picture The early symptoms include pains paraesthesias mild ataxia and bladder disturbance As the disease progresses all these may become more severe and gastric or other visceral crises incontinence of bladder and bowel impotence optic atrophy ocular palsies deafness Charcot joints and ulcers on the feet may appear

The characteristic tabetic pains occur at some stage or other in over 90 per cent of patients They are described as lightning pains or jabs of sharp needles into the muscles or joints and frequently feel horizontal rather than along the axis of the

The aetiology is uncertain It has been suggested that the changes in the nervous system are due to *direct involvement by either the virus of the disease* itself or some other virus activated by the disease but no virus has yet been isolated from the nervous system of patients with this form of encephalomyelitis and the pathological changes are unlike those which occur when the nervous system is directly invaded by any of the known viruses A view that is gaining increasing support is that the condition is *due to an allergic reaction to the antibodies* produced against the infection

Scattered lesions in the brain and spinal cord consisting of areas of demyelination with relative sparing of the axis cylinders are the characteristic pathological change These are common around a distended vein and the condition is usually referred to as perivascular demyelination

Clinical Picture This is related to the portion of the nervous system which is most severely damaged not to the type of vaccination or the nature of the exanthem As any part of the nervous system may be affected many clinical syndromes may occur *The disorder is ushered in by headaches stiffness* of the neck and drowsiness which may pass on to stupor coma and convulsions with motor or sensory hemiplegias and signs of focal cerebral involvment such as aphasia Evidence of acute transverse myelitis complete or incomplete may be found

The cerebro spinal fluid is at normal pressure with between 15 and 250 lymphocytes per mm^3 The *protein is slightly raised The sugar and chlorides* are normal

The mortality rate is approximately 10 to 15 per cent death being due to cerebral damage or intercurrent infection The neurological signs of patients who recover improve to a surprising degree complete resolution being common

Treatment In addition to symptomatic treatment cortisone or its derivatives should be tried in case the hypersensitivity theory is correct. 300 mg of cortisone or *equivalent doses of its derivatives* per day should be given for 2 or 3 days and the dose should then be gradually reduced as improvement occurs

Other Types of Acute Encephalomyelitis

An acute encephalomyelitis of virus origin has been described in many parts of the world It is frequently carried by ticks or mosquitoes may be epidemic or endemic and usually has a mortality of between 15 and 20 per cent The ganglion cells of the nervous system are affected and there is a perivascular demyelination with some haemorrhages

In recent years a number of widely separated outbreaks of a milder type of encephalomyelitis have occurred which have been generally labelled benign encephalomyelitis with myalgia No causal agent has been isolated but the outbreaks have shown a general clinical resemblance and the infectivity in closed communities has been high *Systemic disturbance is usual at the onset* suggesting an illness of invasion and the disorder may stop at this prodromal stage Otherwise in a few days various neurological manifestations develop such as pareses reflex changes cutaneous hypersensitivity and other disorders of sensation and muscle fasciculation and spasm Minor mental disturbances are common The brain stem and peripheral nerves may be involved. The *cerebro spinal fluid is normal* The course of the disease may be protracted and relapsing and complete recovery is the rule though occasionally there has been permanent residual disability There has been no opportunity of studying the pathological changes

Syphilis

Syphilis of the nervous system *is decreasing* partly because primary syphilis is decreasing and partly because early treatment is now so efficient. Cases however still occur and may be divided into three main groups—

1 Asymptomatic
2 Meningeal and vascular
3 Parenchymatous

The first group includes those cases with abnormalities of the cerebro spinal fluid who have *no symptoms or signs* of damage to the nervous system The second and third groups are not so clearly differentiated and may overlap very considerably

The pathology of asymptomatic neurosyphilis is not known but it is presumed that changes are largely confined to the meninges with perhaps mild affection of the parenchyma and vessels in a few cases As there are *no symptoms or signs* the condition is discovered fortuitously when a lumbar puncture is carried out as part of the routine follow up of cases of primary or secondary syphilis or for some other purpose The cerebro spinal fluid *shows a mild or moderate lymphocytic pleocytosis* with a minor rise of protein and slight excess of globulin The Wassermann reaction *is positive* in the blood and cerebro spinal fluid

The treatment is with penicillin as *described below*

Meningeal and Vascular Neurosyphilis

This usually occurs between the second and fifth years after infection It may affect either the cerebral or spinal meninges or the vessels

revert to normal indicating that the disease is no longer active

Diagnosis The diagnosis of tabes dorsalis depends on the presence of lightning pains dysuria and ataxia in association with Argyll Robertson pupils absent deep reflexes and loss of sensation but one only of these symptoms or signs should give rise to suspicion and it is unusual to find them all The condition must be differentiated from a chronic polyneuritis compression of the lower spinal cord or corda equina and subacute combined degeneration of the cord Adie s syndrome has in the past been frequently mistaken for tabes dorsalis Its cause is unknown and it may develop suddenly It is associated with a myotonic pupil most frequently unilateral and usually larger than the normal pupil It may be oval with the long axis either horizontal or vertical The reaction to light direct or consensual is abolished unless the light is very strong when a slow contraction may occur In accommodation convergence contraction of the pupil is slow and perhaps delayed but the pupil may finally become even smaller than the normal one On relaxing convergence accommodation the pupil very slowly returns to its previous size The myotonia may affect the ciliary muscles as well as the muscles of the iris These may or may not be associated absence of the deep reflexes The pupil of Adie s syndrome therefore resembles the Argyll Robertson pupil only very superficially As it is not associated with sensory loss or with characteristic pains and the cerebo spinal fluid is normal confusion should not arise

Treatment Penicillin preceded by a course of mercury iodides and bismuth should be given as described earlier This frequently results in an improvement of symptoms but those due to permanent damage of the spinal cord cannot be affected and lightning pains gastric crises and Charcot joints persist Re education exerci es to control the ataxia are important and good results can be obtained by expert physiotherapists provided the patient has sufficient application to follow the treatment Lightning pains are treated by aspirin or other analgesics If the pain is extremely severe and unilateral cordotomy may be used Visceral crises are difficult to treat They may respond to codeine phosphate by injection in doses of 30 to 60 mg (½ to 1 gr) combined with atropine sulphate 1 mg (1/60 gr) Chloral hydrate and sodium bromide 2 g (30 gr) of each per rectum or phenobarbitone 200 mg (3 gr) intravenously or intramuscularly may help Success has been reported from vagotomy but this is not invariable Cordotomy may have to be considered For the Charcot joints orthopaedic treatment including arthrodesis or splints to stabilize the joint may be necessary The bladder should be kept empty if possible by bladder-contracting drugs such as the choline esters in doses of 1 mg by mouth Catheterization should be avoided if possible and the patient may have to wear a receptacle for constant dribbling If there is infection sulphonamide drugs in small doses continuously such as sulphathiazol or sulphadimidine ½ g twice a day may be tried Perforating ulcers should be protected from trauma and weight bearing and necrotic bone should be removed when healing may occur

General Paralysis of the Insane (Dementia Paralytica)

This is a chronic destructive disease of the cerebrum affecting both the cortex and the white matter leading to a dissolution of mental and physical function The brain is atrophic particularly in the anterior part of the frontal and temporal lobes Over the atrophic areas the meninges are opaque thickened and adherent to the cortex The sulci are widened and contain an excess of fluid The ventricular ependyma is granular Microscopically there is an inflammatory reaction of the meninges and in the perivascular spaces of the brain and spinal cord Degeneration of the cortex is found together with degenerative and reactive changes in the glia and white matter There is a considerable deposition of iron pigment Spirochaetes are scattered through the whole substance of the brain

Clinical Picture The onset is usually insidious with mental symptoms which may simulate those of any type of mental disorder Only those who know the patient well may recognize the changes and even they may do so only in retrospect The first manifestations are usually impairment of intellectual efficiency slight defects in the critical faculties and minor peculiarities of conduct Forgetfulness discourtesy unsound judgment and undue susceptibility self assertiveness or carelessness of personal appearance may appear Depression may alternate with elation and grandiosity Loss of appetite insomnia and restlessness may occur mimicking the psycho neuroses As the condition progresses the behaviour becomes more abnormal and the patient tends to become careless not only about dress and appearance but also about money Excesses of food and alcohol intake and sexual aberrations are common at this stage This pattern known as simple dementia is probably the most common Occasionally the grandiose form with marked euphoria and delusions of exceptional capability occurs The patient may act on these delusions distributing money he does not possess and ordering large quantities of goods Other emotional states may appear leading to depression agitation mania or close resemblance to the Korsakow psychosis Speech

limbs The stabs of pain are each very short but they may recur frequently and become agonizing They usually occur in groups lasting two or three days followed by freedom for days or weeks The lower limbs are the common site though the pains may occur in the back upper limbs or elsewhere Paraesthesias are sensations of numbness tingling or pins and needles in the extremities The patient often says he seems to be walking on cottonwool or has tightness or constriction in the trunk producing a curious girdle sensation Visceral crises may occur anywhere but are most frequent in the upper abdomen and are then called gastric crises They usually start very suddenly with acute pain in the abdomen accompanied by nausea and vomiting They may last for several days at a time and the pain may be so severe as to simulate a perforated viscus The ataxia is typically that due to loss of sense of position in the affected extremities and is mainly present in the lower limbs When mild it may be obvious only in the dark or during the Romberg test when moderately severe it produces an uncertain or slapping gait inco ordination of leg movements and poor equilibrium when very severe walking may be impossible even when the patient is concentrating When the upper limbs are involved there is a little clumsiness in the use of the fingers and the position of outstretched arms cannot be maintained when the eyes are closed Movements of the fingers may occur which mimic athetosis and are often called pseudo athetoid

Pupillary abnormalities occur in approximately 90 per cent of patients A true Argyll Robertson pupil is found in over 50 per cent The characteristics of this type of pupil are meiosis complete absence of response to light however strong normal reaction to the accommodation convergence reflex and impairment of response to sympathetic stimulation The pupil is commonly small and irregular and a partial ptosis of the upper lid associated with a compensatory contraction of the frontalis muscles is not uncommon Optic atrophy due to an interstitial neuritis of the optic nerve occurs in about 20 per cent of cases There is a gradual diminution of visual acuity in one or both eyes with contraction of the visual field causing tubular vision or occasionally central or paracentral scotomas The condition may go on to complete blindness but is occasionally arrested before this stage is reached The optic disc is greyish white in colour with sharply defined edges and the retinal arteries are reduced in diameter Ocular motor nerves most often the 3rd are involved in about 20 to 30 per cent of patients and the auditory nerve on one or both sides in a similar number the hearing being affected more frequently than equilibrium

The ankle jerks are lost in over 90 per cent the knee jerks in over 80 per cent and the arm reflexes in approximately 10 per cent of patients With this, some degree of hypotonia is usually found and the patient may complain of muscular weakness though this is more subjective than objective Wasting of the muscles sometimes develops later

Sensory disturbances are common Superficial sensation is diminished in the central part of the face and perhaps the cheeks over the ulnar surfaces of the forearm over the chest particularly around the nipples around the umbilicus and over the peroneal surface of the legs Not infrequently there is a curious disturbance of pain sensation the pain being felt some little while after the stimulus Loss of pain on compression of tendons particularly the Achilles tendon is common There is also loss of sensation in the viscera particularly in the testicles

Disturbance of bladder control is common and may even be a presenting sign It is mainly due to a loss of bladder sensation the bladder itself becoming hypotonic Distension and overflow incontinence is therefore characteristic and there may be difficulty in initiating the flow of urine and usually inability to empty the bladder completely The rectum may be involved in much the same fashion

Trophic changes are usually a late manifestation and occur mainly in the lower limbs The large joints may become painlessly enlarged with or without effusion increased mobility and deformity (Charcot joints *see* p 520) The spine and upper limbs are much more rarely affected Perforating ulcers which are painless indolent circular sores on the plantar surface of the foot usually develop at the base of the great toe The process may penetrate into the bone or the joint

The disease slowly but firmly progresses at first but the activity gradually fades and in time it becomes stationary The permanent damage however remains and the symptoms and signs may be present even though activity is completely absent Tabes is therefore rarely fatal in itself but death may result from either urinary complications or the trophic changes produced by loss of sensation in the skin

Investigations In early tabes the blood Wassermann reaction is positive and the cerebro spinal fluid shows a mild lymphocytic pleocytosis up to about 50 cells/mm^3 a rise of protein to 60 or 70 mg per cent a positive Wassermann reaction and a so called tabetic colloidal gold curve (in which there is the greatest precipitation in the middle of the curve) As the years pass the cerebro spinal fluid gradually reverts to normal and in advanced cases it may be completely normal in all respects The blood Wassermann reaction too may gradually

and various systemic diseases Syphilis is a rare cause of intracerebral haemorrhage The mechanism of the rupture of diseased vessels is not known Moreover not all intracerebral bleeding is due to rupture of the arteries the veins may also be involved The most common site for a single haemorrhage is in the neighbourhood of the basal ganglia and it extends from this region to the internal capsule and ruptures into the lateral ventricles in about two thirds of the cases Haemorrhage in the lobes of the hemispheres frequently begins at the junction of white and grey matter It may then extend along the corona radiata or association tracts and if not too large may merely separate the fibres without disrupting them If the patient does not die the blood and necrotic brain tissue are removed by phagocytes and replaced by connective tissue and newly formed blood vessels This replacement is incomplete leaving a shrunken area which is filled with fluid though occasionally the clot is treated as a foreign body and a blood cyst is formed

Cerebral Thrombosis

This is most commonly caused by arteriosclerosis but may also be caused by acute or chronic inflammatory reactions around the blood vessels as in syphilis acute or chronic meningitis or encephalitis Rarer causes of cerebral thrombosis are thrombo angiitis obliterans periarteritis nodosa lupus erythematosus states in which there is increased viscosity of the blood (such as polycythaemia leukaemia and dehydration) and mechanical constriction of a blood vessel as by a tumour

When a cerebral artery is occluded there is a complete or relative ischaemia of the brain tissue which it supplies and oedema and congestion of the neighbouring areas The oedema subsides after a few hours or a few days and the ischaemic brain tissue undergoes necrosis usually becoming a pale and shrunken infarct Occasionally there is an influx of red cells into the area resulting in a red infarct which is always swollen for longer than is a pale infarct The necrotic brain tissue is eventually liquified and removed by phagocytic microglia leaving a shrunken scar of newly formed capillaries and glia though sometimes these surround small multilocular cysts filled with a clear fluid

Cerebral Embolism

This occurs when a vessel is occluded by a fragment of clotted blood tumour fat air bacteria or other substance The occlusion results in necrosis of the area supplied exactly as described in cerebral thrombosis The majority of cerebral emboli are sterile but in patients with bacterial endocarditis or septic processes in the lungs the emboli may be infected and a diffuse encephalitis abscess or meningitis may follow

Cerebral embolism is most commonly associated with disease of the heart particularly with auricular fibrillation or coronary thrombosis

Occasionally a clot reaches the brain from the peripheral venous circulation It is difficult to understand how this happens A patent foramen ovale has been implicated though before this can act as a pathway for a clot to reach the cerebral circulation the usual pressure relationships in the auricles must be reversed probably as the result of a rise of pressure in the pulmonary circulation It is presumed also that emboli from the abdominal or pelvic cavities can reach the brain by way of the paravertebral plexus of veins

Clinical Picture of Cerebro-vascular Lesions Focal premonitory symptoms are not very common and usually indicate the onset of a thrombosis rather than a haemorrhage Transient loss of speech hemiplegia paraesthesias affecting one half of the body or hemianopia may precede the onset of severe paralysis by a few hours or days Occasionally these signs are present intermittently for some considerable time They are then thought to be due to relative ischaemia produced either by the fluctuating arterial flow through a gradually occluded vessel or by emboli thrown off from an atheromatous lesion in a carotid artery

In the majority of patients the symptoms of a cerebral vascular accident are of sudden onset and reach maximum intensity within a few minutes to a few hours at the most The symptoms are focal and generalized the focal symptoms being due to the particular site of the haemorrhage or infarct Generalized symptoms include headache vomiting convulsions and coma They may occur in any type of cerebral vascular accident but are commonest with an intracerebral or subarachnoid haemorrhage Coma is present at the onset in about half the patients with a cerebral haemorrhage and may develop shortly after the onset in a further group Convulsions are usually generalized though occasionally focal They occur at the onset or within a few hours in about an eighth of the patients with haemorrhage Vomiting is present at the onset in about 50 per cent of patients with a haemorrhage Headache occurs in two thirds of the patients with an intracerebral haemorrhage and all the patients with a primary subarachnoid haemorrhage who are not comatose

Small haemorrhages or the occlusion of small vessels cause few general signs but large haemorrhages or the occlusion of major vessels usually cause a rise in temperature and an increase in pulse

both receptive and expressive is disturbed parallel with other mental functions and echolalia may occur With deterioration however dementia pre dominates and in the end there may be little evi dence of any mental activity

Physical Symptoms and Signs Fifty per cent of patients have epileptic attacks which may be localized generalized or of the temporal lobe type Occasionally the congestive or apoplectiform type of attack occurs as an initial manifestation with resulting transient evidence of focal disorder such as hemiplagia aphasia apraxia and hemianopia which recovers completely within a week or two The typical Argyll Robertson pupil or some variety of this is usually present Optic atrophy occurs in about a fifth of the patients though it is rarely severe enough to cause a marked loss of visual acuity Voluntary power diminishes and there is associated tremor, which is seen on voluntary move ment in the face lips tongue and the outstretched hands and slurring of speech Inco ordination may occur in the later stages giving an unsteady gait and ataxia of the upper limbs The deep reflexes are usually exaggerated the abdominal responses may be diminished and the plantar responses extensor Sphincter control is disturbed but this is due to the mental changes rather than to affection of the reflex arc (as occurs in tabes) If tabes is also present however the tendon reflexes may disappear and typical sensory changes may then be found

Investigations The cerebro spinal fluid is abnor mal Pressure may be increased and there are up to 100 mononuclear cells per mm^3 The protein content is raised between 50 to 100 mg per cent with an *increase of globulin The Lange colloidal gold curve is of the paretic type* that is the greatest precipita tion is at the beginning of the curve The Wasser mann reaction is positive in the cerebro spinal fluid in all patients and in the blood in from 90 to 100 per cent

Prognosis The prognosis was considerably changed by the introduction of treatment with malaria though this has now been largely super seded by penicillin Previously the disease was in variably fatal usually in 3 to 4 years, though remissions occurred in a few patients The outlook is now very much better, especially if treatment is instituted early

Treatment Penicillin preceded by a short course of mercury iodides and bismuth is now the treat ment of choice as described on page 405 Malaria need not be used unless the patient is resistant to penicillin

Congenital Neurosyphilis

In common with other forms of neurosyphilis this is becoming very much rarer particularly now that ante natal care and treatment in the early stages of pregnancy are the rule

Congenital general paresis usually comes on between 6 and 21 years the average age being 12 or 13 Though the child may have been backward at first development may be normal until puberty when the symptoms begin either suddenly or in sidiously As in the acquired cases the initial symp toms may be either mental or physical The earli st mental changes are in character and intelligence behaviour becoming eccentric and school perform ance deteriorating *Silliness forgetfulness irasci bility and inattentiveness appear* Psychopath behaviour is uncommon Epilepsy is frequent and inco ordination tremors and dysarthria all appear in time There may be peculiar choreiform move *ments or reflex chewing grasping* and sucking The pupils are always altered and optic atrophy with or without choroidoretinitis is much more frequent than in the adult The reflexes become increased and the plantar responses extensor Both the blood and cerebro spinal fluid show changes similar to those of the adult cases Physical development is retarded if the disorder begins early The disease is steadily progressive and usually ends fatally in 2 to 5 years Treatment by penicillin as already des cribed, is less effective than in the adult

Congenital tabes is extremely rare Th signs and symptoms are much the same as in the adult.

Vascular Lesions and Diseases of the Cerebral Blood Vessels

The common types of cerebral vascular lesions are intra cerebral haemorrhage cerebral thrombosis cerebral embolism and primary sub arachnoid haemorrhage *All may occur at any age* but haemorrhages and thrombosis are rare under 40 The peak incidence of thrombosis is in the sixth to eighth decades and of haemorrhage in the fifth to eighth decades

Intracranial Haemorrhage

This is produced by rupture of one of the cerebral vessels in the brain or the meninges and in the vast majority of cases the vessel is arteriosclerotic Haemorrhage may however result from the rupture of congenital or mycotic aneurysms or from acute infections, intoxications trauma blood dyscrasias

lution of all signs within a few hours or days Most commonly the symptoms improve slowly over several months some permanent residuum such as stiffness and difficulty in use of the leg awkwardness in use of the hand or some degree of speech defect being usually left Once a cerebro vascular accident has occurred there is always the risk of recurrence at any time In elderly patients with a severe degree of arteriosclerosis there may be many small cerebro vascular lesions usually thrombotic The vessels involved may be so small that there are few or no general or focal signs More commonly transient attacks of dizziness or slight weakness or numbness of an extremity occur and there may be a gradual progressive failure of mental powers the onset of pseudo bulbar palsy rigidity of the muscles or Parkinsonism

Treatment In the first stage nursing care is important The patient may have to be kept in a semi prone position with the head down particularly if vomiting is occurring to prevent the inhalation of vomit or saliva Frequent changes of position prevent the development of bed sores or hypostatic pneumonia Fluids can be given by mouth or if swallowing is difficult through a nasal tube passed into the stomach The bladder must be emptied by catheter if necessary and the bowel emptied occasionally by enemas or glycerine suppositories If the patient is restless sedatives such as intramuscular paraldehyde 5 to 10 ml may have to be used but care should be taken not to depress the respiratory centre There is no known method of stopping the bleeding from a ruptured vessel venesection being useless Lumbar puncture is not likely to increase the bleeding and may be useful in relieving raised intracranial pressure if there is much blood in the subarachnoid space It cannot help however if the blood is entirely within the substance of the cerebrum and it may even produce coning of the temporal lobes through the tentorial hiatus Operative removal of an intracerebral clot should then be considered The indications for this are not yet absolutely clear but the operation should probably be restricted to those patients who have survived at least 24 hr after the initial haemorrhage and have therefore emerged from the immediate state of shock If the patient is obviously at this stage recovering rapidly nothing is to be gained by surgery but if the condition remains stationary for 24 to 36 hr removal of an intracerebral clot may be dramatic in hastening recovery

Attempts have been made recently to improve the cerebral circulation of patients with cerebral thrombosis by procaine block of the stellate ganglion but it is doubtful if this helps much Vaso dilators such as nicotinic acid intravenously are likewise of uncertain value On the other hand the inhalation of a mixture of 7 to 10 per cent CO_2 in oxygen for five minutes every hour through a B L B mask is thought to be quite helpful as it dilates the cerebral vessels without affecting the general level of blood pressure Anti coagulants are being tried and are probably most useful in cases where transient disturbances of cerebral function give warning of impending thrombosis It is questionable whether they are helpful once a thrombosis has occurred except perhaps by preventing extension of the process into other vessels

After the recovery from the immediate effects of the cerebro vascular accident an attempt at restoration of function in the paralysed limbs must be made This is started while the patient is confined to bed Passive and active movements of the affected limbs are most helpful particularly in preventing changes in the joints Re education is then attempted by appropriately designed occupational therapy Any tendency towards the development of contractures must be dealt with by stretching the affected muscles and by the use of splints at night As soon as possible the patient should be got out of bed and allowed to sit up in a chair beginning with a few minutes and increasing gradually The treatment of speech disorders is extremely difficult and requires tremendous patience both by physician and patient The best results are obtained when re-education exercises are given by a trained speech therapist

COMMON SYNDROMES OF CEREBRAL VASCULAR ACCIDENTS

Common and Internal Carotid Artery

Of recent years the diagnosis of thrombosis of the carotid artery has become increasingly common and it is now realized that even at autopsy this may be missed unless the carotid artery in the neck is examined carefully Careful clinical radiological and autopsy studies indicate that the possibility of internal carotid occlusion deserves consideration in every case in which cerebral infarction seems likely unless some other cause is apparent This rule is applicable whether the lesion is a large one causing massive hemiplegia or so small as to cause focal symptoms only

Internal carotid occlusion sometimes results in repeated transient disturbances of cerebral function which vary both in form and duration Commonly paresis of a limb or of corresponding limbs on

rate The respiration varies but is frequently of the Cheyne Stokes type As arteriosclerosis and hyper tension are the most frequent causes of both haemorrhage and thrombosis evidence of sclerosis of *peripheral retinal vessels* abnormalities in the heart and elevation in the blood pressure are fre quently present Inequality in the size of the pupils is common and the larger pupil is usually on the side opposite to the cerebral lesion The reaction of the pupils to light *is diminished in over a quarter of* the patients with a cerebral haemorrhage but is *much less frequently* diminished in those with a cerebral thrombosis Conjugate deviation of the eyes alone or of the head and eyes together is usual if the lesion is severe especially if it is a haemorrhage De viation is almost always towards the side of the *lesion and is associated* with *impairment of* the movement of the head and eyes in the opposite direc tion This deviation tends to disappear as the patient improves Stiffness of the neck is common in patients with an intracerebral or primary subarachnoid haemorrhage and is due to blood in the cerebro spinal fluid Confusion dis orientation and impair *ment of memory are frequent in the period* immediately following a cerebral vascular accident All the tendon reflexes may be lost and both plantar responses may be extensor in the comatose state immediately following the onset but as the patient improves the evidence of focal brain damage be comes far clearer

A great number of patients have albumen and casts in the urine Occasionally glycosuria occurs due to a temporary disturbance of the sugar meta bolism as a result of the cerebral injury The cerebro spinal fluid is normal in patients with a sterile embolus or a thrombosis apart sometimes from xanthochromia and a few red cells but is blood *stained in all patients with* a *primary* sub arachnoid haemorrhage and in the large majority of *patients with a cerebral haemorrhage* Only in the presence of a septic embolus are the white cells markedly increased When *there is blood in* cerebro spinal fluid the protein content is increased because of this otherwise the protein content is only slightly elevated

Diagnosis The diagnosis of a cerebral vascular *lesion* is made by the sudden appearance of focal or generalized neurological symptoms in a patient *with hypertension* arteriosclerosis or other evi dence of cardiovascular disease The differential diagnosis is *two fold First the symptoms must* be differentiated from those of other lesions of the nervous system Second an *attempt must be made* to determine which form of cerebral vascular acci dent is present and which vessel is involved

From other lesions of the nervous system the diagnosis is usually *not difficult when the complete* history is known but is often very difficult if the *patient is found comatose* and *no adequate* history can be obtained Other causes of coma must be considered particularly injury uraemia diabetes and hypoglycaemia and the excessive intake of alcohol or hypnotics The presence of focal signs of damage must be due *to a cerebral vascular lesion* a cerebral tumour or a focal injury The differential *diagnosis between subdural* haematoma and a cerebro vascular lesion may be very difficult but is important because immediate operation in the former case may be necessary to save the patient's life The situation may be further complicated if the *injury which produced subdural* haematoma was only slight and if weeks elapsed between the *injury and the onset of symptoms produced by the* haematoma In fact the possibility of subdural haematoma should always be kept in mind particu larly in old people chronic alcoholics and the subjects of hypertension If the diagnosis is at all possible *it is important* to confirm or exclude it by arteriography and even exploration

The differential diagnosis between cerebral hae morrhage and cerebral thrombosis or embolus is important chiefly for prognosis both *for life and* for the degree of recovery of focal neurological signs It is also of great importance if the use of anticoagulants is contemplated since cerebral hae morrhage is a complete contra indication Cerebral *embolism is indicated whenever* neurological symp toms suddenly develop in a patient with acute or chronic *endocarditis auricular fibrillation* a recent coronary thrombosis septicaemia or a septic focus There may be evidence of embolic phenomena else where in the body The clinical differentiation between cerebral haemorrhage and thrombosis is extremely difficult and even the most expert can be mistaken Convulsions severe headache nausea or *vomiting at the onset* Cheyne Stokes or laboured respirations conjugate deviation of the eyes stiff *ness of the neck tetraplegia and* bilateral extensor plantar responses all favour haemorrhage A blood stained cerebro spinal fluid is *proof of haemorrhage*

Course and Prognosis The course of the disorder depends on the type of lesion its extent *and* the presence or absence of other complicating factors After haemorrhage of any appreciable size or occlu sion of a major vessel by a thrombus or an embolus the prognosis for life is grave The prognosis for *return* of function of paralysed limbs cannot be predicted with any degree of certainty in the first *few days or weeks* In the non fatal cases there is usually some improvement in the focal neurological signs and *in* some cases *particularly* with small emboli this may be dramatic with complete reso

sensation over the entire half of the body Thrombosis of the anterior inferior and superior cerebellar arteries produces similar syndromes though affecting slightly higher regions of the pons The 5th 7th and 8th nerves on the same side are involved and there are the cerebellar signs on the same side and the crossed sensory signs already described

Pseudo-bulbar Palsy

This is the term applied to weakness or paralysis of the muscles of swallowing and talking due to a loss or disturbance of cortical innervation of the motor nuclei of the medulla As these nuclei are bilaterally innervated only bilateral lesions cause the symptoms The palsy may result from multiple lesions of both hemispheres or of the upper brain stem Multiple cerebral thrombi following cerebral arteriosclerosis are the most common cause Frequently the patient has had a hemiplegia perhaps some years before and then develops another hemiplegia on the opposite side If the interval between the two vascular accidents is long there may have been a partial or complete recovery from the first hemiplegia but a pseudo bulbar syndrome will still occur Pseudo bulbar palsy may occur without paralysis of the extremities if the lesions are sharply localized to the cortico bulbar fibres It may also be due to other diseases involving the pyramidal tracts such as amyotrophic lateral sclerosis and multiple sclerosis In association with the dysarthria and dysphagia there is often loss of emotional control with spontaneous outbursts of laughing or crying which are occasionally paradoxical

If there is difficulty in swallowing a nasal tube into the oesophagus or stomach is needed to maintain nutrition There is always the risk of food being inhaled into the trachea If the syndrome is due to an acute vascular lesion then some recovery of swallowing occurs if the patient lives long enough

Intracranial Aneurysms and Primary Subarachnoid Haemorrhage

The most common cause of bleeding into the subarachnoid space is rupture of meningeal vessels by trauma to the head Haemorrhage into the subarachnoid space may also result from blood dyscrasias intracranial tumours angiomas certain toxic or infectious disorders of the nervous system and intraventricular haemorrhages These are all described as secondary haemorrhages Primary subarachnoid haemorrhage is due to rupture of one of the vessels in the subarachnoid space usually but not always at the site of an aneurysm It accounts for approximately 8 per cent of cerebral haemorrhages and may develop at any age but is most common in the third to sixth decades

The vast majority of aneurysms in the subarachnoid space are produced by a congenital weakness of the vessel probably due to a maldevelopment of the media particularly at a point of bifurcation Arteriosclerotic changes in the vessels are common in older patients and may be an additional factor in the formation of aneurysms Septic emboli may produce mycotic aneurysms Syphilitic arteritis is a very rare cause Aneurysms vary in size from a small pea to an egg though there are probably fluctuations in the size of them all from time to time Small aneurysms do not cause changes in the nervous system unless they compress one of the cranial nerves Larger aneurysms may erode the sella turcica and base of the skull and compress neighbouring cerebral tissue as well as the cranial nerves An aneurysm may lie free in the subarachnoid space or may be partially buried in the substance of the brain as any intracranial vessel may be the site of an aneurysm Fifty per cent of them are on the internal carotid or middle cerebral arteries and the vast majority are near the base of the skull but they may be found also in the Sylvian or other fissures of the hemispheres Larger aneurysms may be partially or completely filled with organized clot and are occasionally calcified Aneurysms are usually single but in a few cases are multiple

Clinical Picture The symptoms of intracranial aneurysms may be due to compression of the cranial nerves or cerebral substance and to leakage from or rupture of the aneurysm In most cases the aneurysm is silent until bleeding occurs Chronic headache or periodic headache of the migraine type occurs in a few cases but whether this is due to the aneurysm or to coincidental migraine is uncertain

The onset of symptoms is sudden in over 90 per cent of cases and is due to a leakage from or a rupture of the aneurysm The bleeding is only occasionally related to trauma or to physical exertion in most patients it begins spontaneously Pain in the head is the usual initial symptom and may come so suddenly that the patient thinks he has been struck Stiffness of the neck and Kernig s sign occur in practically all cases within a few hours Loss of consciousness at the onset is of grave prognostic significance Hemiplegia monoplegia or aphasia develop immediately or within a few hours in about a sixth of the cases as a result of bleeding into the substance of the brain as well as into the subarachnoid space Convulsions usually generalized occur at the onset in about 15 per cent of cases Mental confusion delirium or lethargy are usual Severe headache is always present It may

opposite sides develops but the weakness may be restricted to the fingers or the face Dysphasia may be the most prominent symptom Paraesthesias may occur with or without paresis The more localized the disturbance of function the shorter as a rule is its duration which may be only a few minutes A hemiparesis may last many hours In the early stages recovery may be absolutely complete after each episode but with repetition signs of persistent loss of function usually appear and the end result is a hemiplegia either as a sudden event or the effect of cumulative paresis Sometimes the progress of the lesion is so slow as to mimic a cerebral neoplasm Occasionally a hemiplegia is associated with ipsilateral blindness which may remain even after the hemiplegia has improved considerably

The diagnosis can be established at the bedside only when a sudden hemiplegia or focal lesion is associated with a weak or absent carotid pulse in the neck The diagnosis can be confirmed by arteriography though this is not without danger It must be remembered however that at autopsy the internal carotid can be found completely occluded on one or both sides without the patient being aware of any abnormal manifestations during life This occurs when the arteries of the circle of Willis are unaffected and the circulation maintained by the remaining patent feeding vessels

Treatment Treatment varies according to whether the occlusion is complete and a permanent hemiplegia has resulted or whether there are intermittent attacks of weakness In the former case the treatment is on general lines as already described In the latter case however anti coagulants may be used in the hope of preventing complete occlusion Recently resection of the partially occluded carotid artery has been attempted with the substitution of an arterial graft Cases have been reported of complete relief of the intermittent attacks of cerebral dysfunction by this means

Anterior Cerebral Artery

Thrombosis usually gives rise to paralysis and sensory loss affecting chiefly the leg on the opposite side If the dominant hemisphere is affected mental confusion clouding of consciousness and aphasia may be added

Middle Cerebral Artery

Occlusion of the main trunk causes infarction of a large part of the cerebral hemisphere producing contralateral hemiplegia hemianaesthesia and homonymous hemianopia If the dominant hemisphere is involved global aphasia—a combination of receptive and expressive aphasia—is also present The face and arm are often more completely paralysed than the leg The arm particularly the hand and fingers also recovers least

Posterior Cerebral Artery

If the whole artery is involved a homonymous hemianopia on the contralateral side develops though the macular region may be spared Frequently there is also a thalamic syndrome due to involvement of the thalamo geniculate artery which is a branch of the posterior cerebral This gives rise to a fleeting hemiparesis or hemiplegia of the flaccid type impairment of superficial and loss of deep sensation spontaneous agonizing burning pain and choreo athetoid movements ataxia or tremor

Basilar Artery

The syndrome here varies according to the site of the lesion in the basilar artery If the whole artery is involved coma soon develops and death usually occurs in two to five days If part of it is involved the pupils are usually small and fixed to light and there may be a variable ocular motor type of palsy Facial and other cranial nerve palsies are present and pseudo bulbar symptoms are common with dysarthria dysphagia bilateral facial weakness and paralysis of the tongue There may be hemiplegia or tetraplegia Cross paralysis with involvement of one of the cranial nerves and paralysis of the opposite side of the body is occasionally seen

Occasionally however only a pontine branch of the basilar artery is involved with lesions towards the middle line of the brain stem producing various cranial nerve palsies associated often with cross hemiplegias As with the internal carotid transient failure of blood flow through the basilar artery may occur producing only short lived symptoms such as diplopia vertigo or difficulty in swallowing These may precede complete occlusion of the whole artery or one of its major branches

Cerebellar Arteries

The long vessels which supply the lateral area of the brain stem also supply the cerebellum and thrombosis of these vessels causes symptoms of dysfunction of the cerebellum and of the nuclei and tracts of the lateral portion of the brain stem The posterior inferior cerebellar artery is most often thrombosed resulting in the sudden onset of intense vertigo and headache together with a marked disorder of equilibrium Other features are on the side of the lesion weakness of the palatal muscles causing dysphagia and dysarthria impairment of pain and temperature sensation in the face Horner s syndrome (with nystagmus) and cerebellar dysfunction in the arm and leg on the side opposite to the lesion impairment of pain and temperature

part of the cerebral circulation this is the internal carotid on the appropriate side Ligation of the internal carotid must not be performed until the circle of Willis is shown to be sufficiently patent to carry on the cerebral circulation This can be done by arteriography with occlusion of the oppo site carotid A further test is manual compression of the carotid for gradually increasing periods up to as long as 30 to 40 min If no symptoms develop it is probably safe to ligate the internal carotid artery although even in these cases contralateral hemiplegia has occasionally developed The alterna tive method of treatment is to expose the aneurysm and to remove it completely if possible or failing this to ligate both the incoming and outgoing vessels This may be extremely difficult technically and the mortality is considerable A large enough series has not yet been dealt with by these means to make it possible to compare conservative and surgical treatment

Carotid Cavernous Sinus Aneurysm

Arteriovenous aneurysm produced by rupture of the internal carotid artery into the cavernous sinus may arise spontaneously or follow trauma It gives rise to a unilateral pulsating exophthalmos with oedema of the eyelids conjunctiva and cornea and sometimes with papilloedema There is a loud sys tolic murmur audible to the patient and on auscul tation over the skull which is suppressed by com pression of the ipsilateral carotid artery There may be a complete or partial ophthalmoplegia of the affected eye The other eye may also become in volved blood being carried by the arterial pressure through the circular sinus into the opposite caver nous sinus The only treatment is ligation of the corresponding carotid artery which usually dimi nishes the symptoms but may produce a residual contralateral hemiplegia

Cerebral Arteriosclerosis

Progressive cerebral ischaemia due to arterio sclerosis leads to impairment of cerebral function before actual blockage of vessels occurs The onset is often insidious and the course slowly progressive though it may be punctuated by minor or major epileptiform attacks leaving residual focal symp- toms The symptoms differ according to the part of the brain mainly affected though no part of the brain escapes The mental symptoms in mild cases consist of a reduction in intellectual capacity with impairment of memory particularly for recent events and names and emotional instability Rambling reminiscence with confabulation may occur the patient often becomes self-centred and opposed to any kind of change in his environment More severe cases may have delusions with or without a paranoid trend Depression is common and there are attacks of confusion which are made worse by removal from familiar surroundings With further deterioration there may be a profound dementia Generalized psychomotor or focal epi lepsy may occur Aphasia agnosia and apraxia in varying forms are met with and pyramidal lesions may be present affecting one or all the limbs and leading to pseudo bulbar palsy Senile tremor is common and involuntary movements may be superimposed upon weakness Arteriosclerotic Par kinsonism may occur

Diagnosis The widespread disorder and the multiple lesions usually suffice to differentiate the condition from intracranial tumour but general paresis of the insane and pre senile dementia may cause diagnostic difficulty

Course The disorder is progressive though there may be long periods without deterioration

Treatment This is mainly symptomatic but every patient who is suspected of suffering from cerebral arteriosclerosis should be given a full course of potent Vitamin B complex parenterally Many old people gradually diminish their intake of food a profound vitamin B deficiency being produced which accentuates the cerebral arteriosclerosis Epilepsy should be treated with anti-convulsants Phenobarbitone as well as being an anti-convulsant is also useful in combating the insomnia and excitability which are so often present

Trauma

Types of Head Injury

Head injuries may be divided into three groups (1) closed head injuries (2) depressed fracture of the skull and (3) compound fracture of the skull This is only of importance with regard to the actual skull damage the prognosis for life and recovery of function depends on the nature and severity of the damage to the underlying brain and whether infection has penetrated the dura mater

Closed head injuries occur when the skull has not been damaged or only a linear fracture is present There may be no damage to the brain simple con cussion or concussion with either oedema or con tusion and laceration of brain tissue Depressed

be localized to the occipital region or to one side of the head at the onset and is then of lateralizing value but in later stages it is usually generalized Pain in the lower part of the back and in the legs occasionally occurs and is probably due to blood tracking into the lumbar subarachnoid space The pain in the leg may simulate sciatica Cranial nerve palsies particularly of the 3rd nerve may develop as the result of sudden compression of the nerves or haemorrhage into their sheaths Occasionally there are haemorrhages into the retina which are commonly subhyaloid with a horizontal upper margin and convex lower margin They are characteristic of the condition The tendon reflexes vary according to whether there is a hemiplegia The plantar response may be extensor on both sides even in the absence of paralysis Sudden expansion of an aneurysm of the carotid in the cavernous sinus may press on all the ocular motor group of nerves and the whole or part of the trigeminal nerve whereas an aneurysm of the supraclinoid portion of the carotid may involve the optic chiasm or optic nerve An aneurysm of the posterior communicating artery may give an isolated 3rd nerve palsy and an aneurysm of the basilar artery or its branches may compress any of the nerves in the posterior fossa

Frequently the temperature is moderately raised and the pulse and respiratory rates are slightly increased during the first few days after the haemorrhage The blood pressure is elevated in more than half the patients Glycosuria may be present in the early stages and occasionally there is albuminuria

Investigations The most important findings are in the cerebro spinal fluid The pressure is always increased commonly to the range of 200 to 600 mm of cerebro spinal fluid The fluid is uniformly blood stained the amount of blood being proportional to the amount of the haemorrhage The white blood count and the protein content of the fluid are usually increased in accordance with the number of red cells though occasionally there is a relative increase in the white cells due to the irritating effect of the blood on the meninges If the fluid is allowed to stand the cells settle and the supernatant fluid is straw coloured or xanthochromic as the result of haemolysis of the red cells The xanthochromia disappears in from one to three weeks depending upon the size of the haemorrhage There may be a slight leucocytosis in the blood

Diagnosis The diagnosis of subarachnoid haemorrhage is made from the story of sudden onset of headache and the finding of neck stiffness with or without confusion coma convulsive seizures or paralysis of the cranial nerves or other neurological signs It is confirmed by finding blood in the cerebro spinal fluid Straight X ray of the skull may show an aneurysm if it is calcified and cerebral angiography may demonstrate the source of bleeding either in the form of an aneurysm or an angioma Not all aneurysms can be seen by angiography they may be filled by clot or their necks may be occluded by cerebral haemotoma

Course and Prognosis The immediate mortality rate of the first haemorrhage is approximately *35 per cent* and an additional *15 to 20* per cent die from a secondary rupture within the next few weeks or months If a large aneurysm ruptures death may occur within an hour and approximately a third of the fatal cases die within the first 24 hr and a further third within the first week Some patients may have as many as five or six separat haemorrhages and still survive The clinical course in patients who survive the first few hours varies considerably In some the aneurysm continues to leak slowly and finally ruptures widely after a few days In others the aneurysm seals off only to rupture suddenly again In cases which recover the bleeding stops and there is gradual improvement in the general state of the patient. The confusion gradually clears though a Korsakow like memory defect may be present for a few days The headache gradually decreases in severity becoming intermittent before it disappears entirely in the course of a few weeks Focal neurological signs may persist but more commonly improve to some extent or disappear entirely this is particularly true of the cranial nerve palsies

Treatment. A lumbar puncture will have been carried out to establish the diagnosis This may be repeated in order to reduce the cerebro spinal fluid pressure to normal If the fluid is withdrawn extremely slowly the risk of causing further bleeding is probably very small If the patient is treated conservatively it is usual to keep him flat in bed for at least five weeks and then to allow him up very gradually in the hope of reducing the risk of a second rupture which is most likely within four o five weeks of the first Powerful analgesics may be needed to relieve the headache When the patient leaves hospital it seems reasonable to advise him to avoid activities likely to raise the blood pressure and in particular to avoid straining at stool Otherwise he should be encouraged to live a normal life and certainly not to become a hypochondriacal invalid

Once the aneurysm is localized whether by clinical means or by cerebral angiography surgical methods of sealing it off from the cerebral circulation should be considered in view of the great risk of recurrence of bleeding The least difficult method is ligation of the afferent artery at a distance from the aneurysm If the aneurysm is on the anterior

upon the site and severity of the injury The mortality varies from nil with simple concussion to 40 per cent or higher with severe laceration After concussion there may be headaches dizziness or vertigo in the immediate post traumatic period These usually disappear within a few months but may be prolonged for many months After severe injuries and prolonged coma there is often a long period of mental confusion before the patient becomes completely rational There is almost always a considerable degree of improvement as time passes but permanent sequelae are not uncommon with severe damage

Treatment Non operative treatment consists mainly of general care and nursing While the patient is unconscious he should be kept in the head-down semi prone position so that vomit or blood is not inhaled He should however be turned from side to side The bladder must be emptied and if there is bleeding from any orifices these should be gently swabbed Careful observation must be carried out at frequent intervals to determine variations in the level of consciousness and the development of focal neurological signs The size and reaction of the pupils should be regularly determined Repetitive examination of this kind is essential so that intracranial bleeding is diagnosed as early as possible If coma persists for more than 12 hr the patient should be fed by a nasal tube passed into the oesophagus or stomach Restlessness is treated by intramuscular paraldehyde or phenobarbitone One million units of penicillin daily may be given in the hope of preventing a pulmonary infection Raised intracranial pressure may be reduced by repeated lumbar puncture As soon as the patient passes out of the state of coma and stupor he can be allowed pillows and gradually sit up more and more depending upon his reaction He should soon be allowed out of bed and his activity should be steadily increased during his stay in hospital Convalescence with graduated exercises is most important to obtain a reasonably rapid recovery from the debilitating effects of all but the most minor brain injury Small doses of sedatives such as phenobarbitone or amytal 30 mg (½ gr) twice a day may need to be continued for some months Alcohol should be avoided after any severe brain injury as tolerance is considerably decreased

Operative treatment consists chiefly of scalp toilet Damaged scalp and brain and fragments of bone should be removed and an attempt made to close the dura as early as possible to prevent infection Simple depressed fractures are probably best elevated this can be done as a planned operation

Complications of Head Injuries

Vascular Lesions

Extradural Haemorrhage

This uncommon condition is produced by a tear in the middle meningeal artery or very rarely by bleeding from one of the dural sinuses The clot increases until it occludes the ruptured vessel though before this occurs it will have reached a very large size and may have caused death It is fatal unless treated early

Clinical Picture The classical description of an extradural haemorrhage is that an injury is followed in succession by loss of consciousness a lucid interval (which may last some hours) and a lapse into unconsciousness perhaps accompanied by hemiplegia However if the brain injury has been severe there may be no lucid interval the patient passing from the coma of concussion into that of cerebral compression produced by the haematoma The hemiplegia may be on the same or the opposite side to the haematoma As the cerebral compression increases the pupil on the same side as the clot begins to dilate and may lose its reaction to light

X ray of the skull is of great value because a fracture line crossing the groove of one of the meningeal arteries is almost always present A calcified pineal gland may be seen to be displaced If further evidence is needed angiography usually shows the haematoma with the depression of the cortex

Extradural haemorrhage is one of the most serious complications of head injury If untreated the mortality rate is probably almost 100 per cent and even if treated the mortality may be high unless the diagnosis is made early

The only treatment is to remove the clot through burr holes in the skull and to tie off the bleeding vessel

Subdural Haemorrhage

This is a collection of blood between the dura and arachnoid It is thought to be always secondary to a severe or minor injury to the head but in abnormal conditions of the blood or in cachexia the injuries producing this may be so minor as to be completely lost from the history

Bleeding in the subdural space is almost always venous and is due to tearing of the small veins which pass across the space This usually occurs over the convexity of the frontal and parietal lobes

fractures of the skull are those in which the *pericranium is intact but a bone is fractured* and depressed inwards to compress or injure underlying brain substance Compound fracture indicates that the pericranial tissue has been torn and there is direct communication between the lacerated scalp and the cerebral substance through a torn dura This may be readily visible or hidden if due to a fracture which involves one of the paranasal sinuses or the middle ear

The term concussion is used only when there is presumed to be no structural damage to the brain It implies a transient disturbance of all brain function from which complete recovery can occur The vital functions of the brain stem are rarely disturbed except in severe injury These can be affected however in very severe injuries to such a degree that death results yet on autopsy no structural damage may be found In the majority of cases the brain stem is only mildly involved The blow on the skull produces either a sudden acceleration or deceleration of the brain relative to the skull resulting in traction on or twist of the brain stem which cause the loss of consciousness or concussion It has certainly been shown both experimentally and in crushing injuries of the skull (such as occur in shunting accidents when the head is caught between buffers) that if there is no or little movement of the head and therefore little movement of the brain much greater force is required to produce loss of consciousness and this is usually due to direct damage to brain tissue

The brain may be contused or lacerated even when the skull is undamaged or only slightly damaged The brain injury may be either beneath the site of the blow or in the opposite hemisphere (contracoup injury) Its degree is related to the force of the blow There may be only a minor petechial haemorrhage in the cortex or more extensive haemorrhagic necrosis of the cortex and subcortical white matter with petechiae in the basal ganglia and brain stem Laceration of the arachnoidal vessels produces subarachnoid bleeding or a subdural haematoma whereas laceration of a meningeal vessel produces an extradural haematoma

Perforating wounds are especially common in war time and are frequently not associated with concussion This is probably due to the small size and very high velocity of the missile It may penetrate the skull and even produce a through and through wound without causing any acceleration of the brain relative to the skull Consciousness may therefore not be lost unless a blood vessel is torn and bleeds inside the skull causing a rising intracranial pressure or unless a vital area such as the brain stem is involved

Clinical Picture Transient loss of consciousness is the most important feature of cerebral concussion The period of coma varies from a few seconds to several hours or days depending on the severity of the brain damage In all but the most minor injuries a period of amnesia follows the injury usually called the post traumatic amnesia (P T A) The return of consecutive memory indicates a return of cerebral function to approximate normality The length of the amnesia *i e* the time from the injury to the return of consecutive memory is probably a more valuable measure of the severity of the injury than the actual duration of the coma particularly as it is so difficult to assess the end of the coma period The P T A in mild injuries is less than 1 hr in moderate injuries between 1 hr and 1 day in severe injuries between 1 and 7 days and in very severe injuries more than 7 days In moderate and severe injuries there is usually a loss of memory for a period before the injury This is known as the retrograde or antegrade amnesia (R A) and is rarely more than a few seconds or minutes but is occasionally prolonged to ½ or 1 hr Longer periods than this may be due to hysteria or to such severe brain damage that there is complete loss of previous memory

Post traumatic amnesia is occasionally prolonged by complications not related to the brain damage and may thus give a false idea of its severity Such are toxic states leading to a toxic delirium considerable dehydration vitamin deficiency (particularly in old people) intracranial haematomas and hysteria

On recovering consciousness the severity and nature of the symptoms are related to the degree of brain damage

Investigations X rays may show damage to the skull and may even show air in the subarachnoid space and the ventricles if there is a free communication between the outside air and the subarachnoid space as when a paranasal sinus is injured The cerebro spinal fluid is entirely normal when there has been only a concussion but is blood stained and under increased pressure when there is contusion or laceration of the brain The electroencephalogram shows a suppression of the electrical activity of the cortex at the time of injury With recovery the activity returns to normal after going through a phase in which there is generalized slowing and an increase in voltage Focal damage to the cortex may show evidence of abnormal electrical activity at the appropriate site for many weeks or months after the injury

Course and Prognosis The prognosis depends

Mental Disturbances

Mental changes occur immediately after the re covery of consciousness in all patients who have had severe brain injury passing through the stages of semi stupor confusion and occasionally a Korsa kow like syndrome Later intellectual impairment is common particularly in the old and is often accompanied by personality change Frequently the personality becomes a caricatured exaggeration of what it was previously the less pleasant aspects often being the most exaggerated Alternatively the personality as a whole becomes flattened Focal neurological signs and post traumatic epilepsy usually accompany these changes

The Post traumatic Syndrome

Just under half the patients who have had a head injury complain of headache dizziness insomnia irritability restlessness inability to concentrate ex cessive sweating depression and difficulty in adjust ing themselves to their environment These symp-toms may persist for only a few weeks or may go on for years They are labelled post concussional state or post traumatic neurosis according to whether they are thought to be organic and the direct result of the injury or neurotic manifesta tions the injury acting as a trigger mechanism Both factors probably play a part in the majority of patients The severity of the injury is not directly related to the development of post traumatic symp toms as they may occur in patients who never lost consciousness but they are more common in the patients who lose consciousness and have an amnesic gap The symptoms are certainly more likely to occur in patients who have previously had neurotic symptoms or shown some evidence of in stability such as frequent changes of employment or who come from neuropathic stock The desire to obtain financial compensation or sympathy may produce the symptoms or more probably prolong them once they have developed

Clinical Picture Headaches are common follow ing head injury They are frequently severe and more or less constant at first but usually decrease in severity and become intermittent as time passes In 2 or 3 weeks they may become paroxysmal and consist of a dull aching throbbing or pressure sen sation Occasionally they occur with excitement or concentration Many patients continue to have daily headaches for years but in the majority they diminish and may disappear entirely within 6–12 months

Dizziness is a constant symptom and is found early after the return of consciousness It is often related to movement and severe true rotational vertigo may occur Attacks of true vertigo are probably due to the trauma damaging the vestibular labyrinth The vertigo most commonly develops in a definite position often with the head back and turned to one or other side though there may be a latent period of some seconds after assuming the position before it begins It is always associated with nystagmus This vertigo can be helped by head exer cises as are used following labyrinthectomy and by anti vertiginous substances such as promezathine (Phenergan) Avomine cyclizine and prochlo perazine (Stemetil) However the so called dizziness of which some patients complain is a feeling of insecurity and unsteadiness not associated with true rotational vertigo This phenomenon is never associated with nystagmus and usually does not respond to the same treatment as the traumatic positional vertigo

Insomnia is frequent sleep is difficult to obtain and is restless when it occurs Often there are terri fying dreams particularly in relation to the events of the accident This disturbance lasts for as long as the other symptoms and should be treated by sedatives or hypnotics

Irritability restlessness concentration difficulties and depression are common The patients cannot stand noise cannot enjoy themselves have little control of temper or emotions and are a burden to themselves and their families If there is no actual intellectual impairment most of these symptoms usually improve with time If however there is intellectual impairment the personality change may be of organic origin and improvement is then very slow and incomplete

Sweating is less common than the other symp toms though not infrequent and is often associated with other evidence of vasomotor instability

The outlook is difficult to forecast Progressive recovery usually occurs though headache and ver tigo often persist for up to 6 months before there is much improvement Undoubtedly the prognosis is very markedly affected by the patient s previous personality the more stable the patient the greater the degree and rapidity of recovery

Treatment The most important immediate aid to recovery is an encouraging attitude by both doctors and nurses No two patients can be treated in exactly the same way and it is impossible to lay down rigid rules as to the length of time that should be spent flat in bed and the rate at which exercise can be introduced To many patients an injury to the head is much more serious than an injury to any other part of the body Fears of permanent damage or of insanity either now or in the future are common These fears should be combated by repeated re assurance and an optimistic environment and a full

It is rarely found in the posterior fossa and diagnosis of posterior fossa subdural haematoma is extremely difficult The haematoma is bilateral in 15 per cent of cases

The blood extravasated into the subdural space is not absorbed but is organized or encapsulated and the cerebral cortex is compressed and moulded by the clot Occasionally the clot increases slowly in size because it attracts fluid from newly formed blood vessels The brain will then herniate through the tentorium with damage to the brain stem and cranial nerves producing unusual and false localizing signs

Clinical Picture Subdural haematomas may be either acute or chronic according to whether they occur very soon after the injury or some considerable time later An acute subdural haematoma gives much the same symptoms and signs as those of a fairly severe cerebral laceration Such a haematoma may be suspected when there is fluctuation in the level of consciousness and a hemiplegia It can be found however quite unexpectedly when burr holes are made in the skull of a patient who is not recovering satisfactorily from a head injury

The symptoms of chronic subdural haematoma may date from an injury but this may have been slight and forgotten Intermittent headache slight or severe impairment of intellectual function and fluctuating degrees of stupor are usual and hemiparesis occurs occasionally The condition may mimic any expanding intracranial lesion and it is frequently mistaken for a neoplasm False localizing signs produced by the upper brain stem being squeezed at the tentorial hiatus are common

X rays are only of value when showing displacement of a calcified pineal The electroencephalogram may show a suppression of the electrical activity of the affected hemisphere and if the haematoma is in the parietal or occipital region there may be complete absence of electrical activity on that side Carotid angiography showing a depression of the cortex is diagnostic

Treatment The treatment of subdural haematoma is evacuation of the clot and if possible removal of the surrounding membrane by opening the skull Since subdural haematoma is frequently bilateral both sides should probably always be explored

Infections

Infections within the skull following injury occur when the dura has been torn and organisms get into the subarachnoid space from without Th infection may be introduced at the time of the injury as when a missile penetrates the brain carrying with it hair scalp and bone or when a fracture of a paranasal sinus wall tears the dura allowing air to enter the subarachnoid space The latter condition can be suspected when a cerebro spinal fluid rhinorrhoea or otorrhoea occurs and an X ray may show the air within the cranium

The treatment is to give anti bacterial drugs while operative removal of the infected material or closure of the torn dura is carried out

Sequelae of Head Injuries

Epilepsy

Epilepsy is not common as an immediate result of head injury and when it occurs the head injury has possibly acted as a trigger mechanism in precipitating idiopathic epilepsy On the other hand it may be related to actual cerebral laceration to meningitis or particularly to a post traumatic brain abscess A true post traumatic epilepsy does not usually develop until several months after the injury about a year being the average time All epileptic variants except classical petit mal may occur generalized attacks being more common than focal attacks The incidence of epilepsy varies in different series In closed head injuries when the dura has not been penetrated it is given as between 2 5 and 5 per cent and naturally the more severe the injury the more likely is epilepsy to occur When the dura is penetrated and the brain substance is lacerated the figures are as high as 50 per cent The laceration results in a scar adherent to the dura and the cortex immediately adjacent to the scar probably becomes the epileptogenic focus Attacks which occur in the first few days or weeks after injury usually cease later On the other hand the attacks due to an epileptogenic scar or to a brain abscess rarely diminish

Routine anti convulsant treatment is justifiable for all patients who have suffered severe head injury particularly if a persistent focus of abnormality remains in the electroencephalogram When post traumatic epilepsy has developed treatment by anti convulsants is the same as that for idiopathic epilepsy If after a thorough trial the epilepsy persists operation can be tried provided electrocorticography has delineated the actual focus beyond doubt This focus is then excised whether or not it includes the actual scar Anti convulsants should be given for 2 or 3 years following the operation The results are good in about 50 per cent of patients

by a concentric diminution in the peripheral field and a gradual diminution in the visual acuity which may go on to blindness

Retrobulbar Neuritis This is an acute affection of the optic nerve with gross loss of visual acuity with or without visible changes in the fundus It is most often due to a demyelinating disease such as multiple sclerosis It is interesting that the loss of visual acuity is completely out of proportion to the visible changes in the optic disc Most frequently the visual defect is a central or paracentral scotoma which may be of varying depth and size Usually it is unilateral though it may occur also in the other eye at the same time or later It is often accompanied by slight pain particularly on movement of the eyeball or on pressure If the lesion is near the chiasm the fundus appears normal but when it is near the nerve head the optic disc is swollen or choked with haemorrhages round it The visible changes however are very much less but the reduction of visual acuity is very much greater than in papilloedema though this may seem much more striking When not due to a demyelinating disease retrobulbar neuritis may be associated with blood disorders or changes usually of a septic nature in neighbouring structures such as paranasal sinuses or the teeth The condition usually improves fairly slowly and vision returns to normal but a permanent scotoma of varying size may be left which is often associated with some pallor of the disc particularly in its temporal half

Optic Atrophy This occurs in the following main conditions—

1 Familial disorders usually involving other parts of the nervous system such as the hereditary ataxias and cerebro macular degeneration The eye alone may be involved as in Leber s hereditary optic atrophy or Retinitis Pigmentosa

2 Following ischaemia of the retina

3 Following papilloedema

4 Following inflammation and demyelination *i e* as a sequel to retrobulbar neuritis or syphilis

5 Following trauma

6 Following pressure on the chiasm or optic nerve

7 Toxic amblyopia due to tobacco metals organic compounds methyl alcohol and other poisons

Pressure on the optic chiasm may be due to a pituitary tumour below or a suprasella or hypothalamic tumour above Aneurysms may also compress the optic chiasm and tract A chiasmal arachnoiditis has been described though it is very rare It results in a thickening of the membranes around the optic chiasm and optic tracts There may or may not be a history of previous meningeal affection or head injury

Toxic Amblyopia This may be due to alcohol and tobacco and is most common in middle aged or elderly men who smoke a pipe and drink alcohol in moderate or large quantities It produces a central or paracentral scotoma for colour which gradually progresses to a complete central scotoma The peripheral fields of vision are normal The only treatment is absolute withdrawal of alcohol and tobacco which usually results in an improvement except when the condition has advanced so far that the retinal cells or optic nerve have completely atrophied

Ocular motor Group of Nerves

These are the oculo motor or 3rd the trochlear or 4th and the abducens or 6th nerves Lesions of these nerves as of all other motor nerves may occur at the nuclei of origin in the intramedullary course in the course to and through the meninges and in their peripheral distribution

Complete lesions of the 3rd nerve paralyse the extrinsic muscles of the eye supplied by it (internal superior and inferior rectus inferior oblique and levator palpebrae superioris) The constrictor of the pupil and the ciliary muscles are also paralysed There is therefore ptosis of the upper lid with inability to open the eye The eyeball is deviated outwards and slightly downards The pupil is usually widely dilated and there is no reaction to light or to convergence accommodation Lesions of the 4th nerve paralyse the superior oblique muscle and prevent the eye from being turned downwards and outwards though this defect may be partly compensated by the external and inferior rectus muscles Lesions of the 6th nerve paralyse the external rectus muscles and result in deviation of the eye inwards and diplopia when looking in all directions except to the side opposite to the lesion

Damage to the nuclei of origin of these nerves may be produced by anterior poliomyelitis local vascular lesions brain stem encephalitis or acute thiamine deficiency as in Wernicke s encephalopathy The cells may also be affected by tumour pressure or brain stem compression In the intramedullary course vascular lesions patches of demyelination and encephalitis may affect the fibres In the intracranial course diseases of the meninges and skull basal tumours and aneurysms and thrombosis of the large venous sinuses at the base may all produce lesions Injury with or without fracture of the skull may also involve these nerves Sometimes isolated palsies of one of the ocular motor nerves occur for which there is no apparent cause and which clear

explanation of the nature of the injuries should be given as soon as the patient has improved sufficiently to understand it While the patient should be kept quiet for a number of days after any moderately severe injury, he should not be kept too long lying flat or too long in bed as this increases the risk of psychogenic overlay Even while in bed activity should be encouraged, probably of the simple occupational therapy type Once the patient is out of bed he should be kept fully occupied during the day part of the time being spent in graduated exercises designed to build up the muscles and overcome the asthenia which occurs after any head injury Part time work should soon be started and full time work is usually possible after a few more weeks Small doses of sedatives such as phenobarbitone 15 to 30 mg (¼–½ gr) 2 or 3 times a day or amylobarbitone in similar quantity are frequently helpful Aspirin or compound aspirin phenacetin and codeine tablets are useful for headaches The patient should be encouraged to settle any compensation claims as soon as is practicable Physical rehabilitation in a residential centre if possible is helpful in speeding the patient s return to a full life

LESIONS OF THE CRANIAL AND PERIPHERAL NERVES

Cranial Nerves

Olfactory Nerve and Tracts

Disturbance of smell occurs as a result of injury to the olfactory bulb or its filaments or the central connexions Temporary impairment is frequently due to the common cold or any other condition which causes oedema and closes off the olfactory cleft in the nose Damage to the neurogenic structures may occur when fractures of the anterior fossa tear the filaments of the olfactory nerve as they come through the cribriform plate These may also be torn off by contracoup injuries when the patient receives a blow in the occipital region Inflammations of the dura as in syphilitic or tuberculous meningitis may cause damage to the filaments or to the olfactory bulb The bulb or tract may be compressed by tumours in the neighbourhood such as olfactory groove meningiomas metastatic tumours aneurysms in the anterior fossa or infiltrating tumours of the frontal lobe

Parosmia or perversion of the sense of smell is not often associated with impairment of smell but is usually due to lesions of the temporal lobe Hallucinations of smell may form the aura of convulsive seizures (uncinate fits) This type of aura is invariably unpleasant and cannot usually be described by the patient Hallucinations of smell may also occur in psychoses

Optic Nerve and Tract

Changes in the retina or optic nerve may be the result of trauma or damage by toxins or such diseases as diabetes mellitus leukaemia anaemia and polycythaemia nutritional deficiencies generalized arteriosclerosis and temporal or giant cell arteritis The demyelinating diseases the heredo degenerative diseases of the nervous system local conditions in the eye (such as glaucoma) tumours congenital anomalies and thrombosis of the veins or arteries of the retina may also be accompanied by damage to the retina or optic nerve Changes in the nerve may be due to pressure or infiltration by tumours or aneurysms and by increased intracranial pressure from any cause

Papilloedema This term means only oedema of the optic nerve head and it can be due to many causes The most important is raised intracranial pressure Others are retrobulbar neuritis vascular disease particularly progressive hypertension and obstruction of the circulation through the retinal veins from thrombosis or pressure from without and occasionally blood diseases

The cause of papilloedema in raised intracranial pressure is still under discussion The most favoured hypothesis—that of Paton and Holmes—is that the raised pressure is transmitted along the subarachnoid space around the optic nerve causing compression of the central retinal vein and obstructing the lymphatic drainage from the retina and nerve

The ophthalmoscopic appearances of early papilloedema are congestion of the retinal veins and a little increase in the pinkness of the optic disc The edges of the disc become blurred and gradually the physiological cup is filled Later the nerve head swells and projects above the retina and the oedema may spread to the macula The veins become very engorged and haemorrhages develop round the disc If the swelling persists atrophy of the disc follows The disc becomes paler the swelling diminishes and the arteries become constricted The end result is a flat greyish white disc with indistinct edges and narrow arteries

The visual field changes caused by papilloedema alone are an enlargement of the blind spot followed

lieved by the injection of alcohol into the Gasserian ganglion or individual sensory branches of the nerve Operative procedures (such as cutting the sensory root either in whole or in part or cutting one of the peripheral divisions as it leaves the Gasserian ganglion) carry little risk and give very good results Whatever method is used of putting the nerve out of action paraesthesias of many kinds may develop in the numb region and some patients find these much more difficult to tolerate than the original pain

Facial or 7th Nerve

The facial nerve as it leaves the brain stem is accompanied by the nervus intermedius which carries taste fibres from the anterior two thirds of the tongue and secretor motor fibres to the sub maxillary and spheno palatine ganglia which supply the salivary and lachrymal glands The facial nerve itself supplies motor fibres to the facial muscles Lesions of the facial nerve between the brain stem and geniculate ganglion therefore paralyse all the facial muscles and cause loss of taste on the anterior two thirds of the tongue and a disturbance of the secretion of the lachrymal and salivary glands Lesions between the geniculate ganglion and the point at which the chorda tympani leaves the facial nerve give rise to the same effects apart from the lachrymal secretion Lesions in the region of the stylomastoid foramen cause facial palsy alone Supranuclear lesions of the facial nerve that is lesions above the facial nucleus in the brain stem cause a partial paralysis of the muscles much more severe in the lower half of the face though the upper half is to some extent affected Lesions of the branches of the facial nerve may occur distal to its division in the neighbourhood of the parotid gland causing partial paralysis

The facial nucleus may be damaged by neoplasms inflammatory and vascular lesions demyelinating processes poliomyelitis and motor neurone disease Within the skull the nerve may be damaged by neoplasms aneurysms meningeal infections deposits in blood dyscrasias and in the reticuloses and the herpes zoster virus Inflammatory disorders and fractures of the petrous bone Paget s disease and neoplasms of bone may involve the nerve in its course through the bone Polyneuritis from various causes may affect the facial nerve in common with the other cranial nerves The nerve may be damaged during surgical intervention for conditions which occur along any part of its course Stab wounds gunshot wounds and the pressure of obstetric forceps during delivery are rare causes of damage

Bell s Palsy In most cases there is no apparent cause for facial palsy which is then called Bell s palsy It is said to follow exposure to cold and may be due to swelling of the nerve within the fallopian canal or swelling of the periosteum in the same region

The onset of a Bell s palsy may be accompanied by a feeling of pain behind the ear though this is never severe except when the paralysis is the result of herpes zoster Often the patient complains of a feeling of stiffness in that side of the face and of dribbling from that side of the mouth The paralysis frequently progresses for 24 to 36 hr

When the damage to the nerve is severe the palsy is obvious even when the face is at rest with sagging of the muscles of the lower half of the face and occasionally the lower eyelid The normal wrinkles and folds are ironed out and the palpebral fissure is wider than normal There is a complete absence of all voluntary and associated movements of the facial and platysma muscles and any attempt at movement such as smiling opening the mouth or showing the teeth causes the facial muscles to be pulled to the opposite side Saliva and food collect on the paralysed side The patient cannot close the eye and when he attempts to do so the eyeball is rotated upwards and slightly inwards If the lesion is peripheral to the geniculate ganglion the lachrymal fibres are spared and there is usually an excessive collection of tears Taste on that side of the tongue is affected if the lesion goes back to the origin of the chorda tympani nerve Partial lesions of the facial nerve give the same signs though to a lesser degree

The rate and degree of recovery depend upon the severity of the lesion Most cases recover partially or completely When there is complete recovery the nerve has probably been only functionally blocked no actual severance of fibres having occurred Here recovery usually begins to show itself within three or four weeks and may be complete in six to eight weeks the two sides of the face then being symmetrical When the lesion has been more severe and actual degeneration of fibres has taken place signs of recovery rarely appear under four to five months and recovery is almost always incomplete There is often a tendency for contracture to develop on the paresed side On inspection there may then seem to be weakness of the muscles on the normal side because at rest the face is pulled over by the contracture though as soon as the patient moves his face the weakness becomes obvious Associated movements may occur the mouth twitching every time the eyelids blink and the eye shutting every time the teeth are shown Occasionally there is an excess secretion of tears when the salivary glands are activated in eating (crocodile tears)

up completely The important differential diagnosis is from myasthenia gravis

The cranial nerve most often affected by raised intracranial pressure is the 6th nerve or abducens This vulnerability is probably due to its extremely long course between its emergence from the brain stem and the external rectus muscle The 3rd nerve is only rarely damaged by increased intracranial pressure except when this is of sudden onset Herniation of the uncinate gyrus of the temporal lobe through the tentorial hiatus then results the 3rd nerve being compressed at this point This frequently occurs in massive intracerebral or extradural or subdural haematomas Such ocular palsies may therefore give rise to false localizing signs

Trigeminal or 5th Nerve

Injury to the 5th cranial nerve causes paralysis of the muscles of mastication with deviation of the jaw towards the side of the lesion loss of all forms of sensation in the face and loss of the corneal and jaw reflexes Lesions in the pons usually involve the motor and main sensory nucleus together, producing paralysis of the muscles of mastication and loss of light touch sensation on the face Lesions in the medulla affect only the descending root and produce loss of pain and temperature sensation which is most marked in the forehead and least marked in the chin and usually loss of the corneal reflex The trigeminal nerve may be injured by trauma neoplasms aneurysms, or meningeal infections and it may be involved in a generalized polyneuritis Within the medulla the descending root and its cells of origin may be damaged in syringobulbia multiple sclerosis vascular accidents and neoplasms

Trigeminal Neuralgia

The aetiology of this neuralgia is completely unknown Trauma and infections of the teeth jaw and nasal sinuses have all been incriminated but in the great majority of cases there is no organic disease of the 5th nerve or central nervous system Occasionally the nerve is pressed upon by an adjacent tumour or other lesion the clinical picture being identical with that of idiopathic trigeminal neuralgia

This is the most frequent of all the neuralgias It usually occurs in middle or late life but may occur at any age It is a little more common in women than in men

Clinical Picture The pain of trigeminal neuralgia occurs in paroxysms Between attacks the only symptoms may be those due to fear that an attack is impending. The pain is described as searing or burning and it comes on in lightning like jabs which are confined to the distribution of one or more branches of the trigeminal nerve The second and third division are more frequently affected These jabs may follow one another to give a paroxysm which lasts from a minute or two to 15 or more minutes The frequency of paroxysms varies from many times daily to several times a month The pain is accentuated by talking chewing cold winds washing or shaving The patient may complain of hyperaesthesia of the face Usually there is a trigger zone which when stroked quite lightly will produce a typical paroxysm

As a rule there are no physical signs though occasionally if the patient is examined very shortly after an attack an area of minor anaesthesia may be found

Differential Diagnosis Pain from the teeth and nasal sinuses differs from trigeminal neuralgia and it is important not to confuse them since removing good teeth from the patient with trigeminal neuralgia is a deplorable error Herpes zoster may simulate trigeminal neuralgia at first but the vesicles will establish the correct diagnosis Glossopharyngeal neuralgia may be confused with neuralgia of the mandibular division of the trigeminal However the pain of glossopharyngeal neuralgia is felt in the tonsillar fossa and deep in the inner ear which should distinguish it The pain may also be abolished by painting the affected tonsillar region with 10 per cent cocaine enabling the patient to swallow without pain in a short while Neuralgic migraine and temporal arteritis may both cause pain very similar to trigeminal neuralgia Changes in the temporo mandibular joint as a result of an abnormal bite are another cause of pain in the face

Course and Prognosis The course of trigeminal neuralgia is characterized by remissions The paroxysms of pain may last for a few weeks or months and then cease quite spontaneously The remission may be short or last for months or even years As time goes on the attack free intervals tend to become shorter and may even disappear completely Although the affection is never fatal in itself frequent paroxysms and the fear of an impending attack may both incapacitate the patient Most patients bear their pains well

Treatment Medicinal treatment of trigeminal neuralgia is of doubtful value though if it happens to coincide with a period of natural remission the cure will undoubtedly be attributed to the particular therapy used at that moment Inhalations of trichlorethylene have been used to abort an attack but their effect is quite unpredictable Most analgesics are useless Recently anticonvulsants have been found useful and it is always worth trying phenytoin 0 1 g t d s or primidone 0 25 g t i d The pain of the neuralgia can be completely re

and difficult Sedatives such as phenobarbitone are probably helpful Destruction of the cochlea or division of the cochlear nerve may be tried in the very severe cases though these procedures are not always successful in relieving tinnitus while invariably causing complete deafness

Vestibular Nerve

Lesions of the vestibular nerve produce vertigo disturbance of equilibrium and impairment of ocular movements The most severe manifestations occur when one labyrinth or nerve is partially damaged whereas complete destruction causes symptoms only in the acute stage which soon subside Moderate or severe ataxia occurs if both labyrinths or nerves are affected The symptoms of vestibular damage may occur as an isolated event in an acute labyrinthitis or as recurrent attacks in Ménière s syndrome

Vertigo Vertigo is an awareness of a disordered orientation of the body in space It may be an hallucination of movement of the outside world often rotatory though sometimes oscillatory or a *feeling that the body itself is moving either in* rotation or as a sensation of falling With it the postures and movements of the limbs especially the lower limbs are felt to be ill adjusted and unsteady and there may also be forced movements of the body such as falling or disorientation of part of the body itself as shown by nystagmus occasional diplopia and pass pointing With all but the slighter attacks of vertigo there are often visceral disturbances such as pallor sweating alterations of pulse rate and blood pressure nausea vomiting and diarrhoea There may be a transient loss of consciousness though more often there is a temporary amaurosis

Vertigo can be produced by conditions which affect the peripheral end organs such as drugs impairment of the blood supply (as in atheroma) vasomotor instability or raised intracranial pressure It is a feature of motion sickness (*see* p 538) and may also be due to head injury herpes zoster of the geniculate ganglion acute lesions of the 8th nerve and vascular or inflammatory lesions of the labyrinth Slowly developing conditions such as an acoustic neuroma often do not produce much vertigo though they may produce a great deal of ataxia Finally vascular neoplastic demyelinating or inflammatory lesions within the brain stem may produce severe vertigo

Recurrent Aural Vertigo or Meniere s Syndrome

There are probably many pathological causes of this condition though it has been suggested that its immediate cause is abnormal water retention within the labyrinth Its characteristic feature is recurrent attacks of severe vertigo leading to vomiting and prostration often associated with distortion of sounds tinnitus and increasing deafness. It may gradually clear up or may continue indefinitely recurring frequently

The patient has usually suffered from slowly progressive deafness and tinnitus in one or both ears and then suddenly develops vertigo This may develop so rapidly that the patient falls or it may take some minutes to come on in which case the patient can usually lie down and so prevent himself falling The vertigo is intense and is soon associated with severe nausea and vomiting and occasionally with diarrhoea The attack may last from a half hour to many hours and then gradually improves If the patient attempts to stand and walk he is unsteady and staggers During the attack he prefers to lie on the sound side there is severe horizontal or rotary nystagmus most evident on looking towards the affected ear and deafness and tinnitus are usually intensified Between attacks giddiness may be brought on by sudden movements of the head. *The attacks tend to recur at irregular intervals and* are of varying severity As the deafness increases the attacks gradually diminish Between attacks nystagmus is absent, but there is perception deafness and diminution of the response of the vestibular organs to caloric stimulation.

Treatment. In an attack all that can be done is to give anti vertigo substances parenterally Of these promezathine (Phenergan) 25 to 50 mg or chlorpromazine in similar doses are extremely useful. Between attacks mild sedation by phenobarbitone 30 mg (½ gr) two or three times a day or small doses of promezathine or chlorpromazine can be tried Salt free diet together with restriction of fluid intake to two pints a day can be helpful Vasodilators such as nicotinic acid 100 mg three times a day before meals infusions of histamine or stellate ganglionectomy occasionally help If none of these remedies is effective and the hearing is severely affected the labyrinths can be destroyed by the injection of alcohol into the inner ear after it has been exposed If the hearing is reasonably well preserved which is unusual this operation is rash since the other side may later be involved and a better operation is the intracranial division of the vestibular fibres of the 8th nerve

Glosso-pharyngeal or 9th Nerve

The 9th nerve contains some motor fibres but is mainly sensory The motor fibres are supposed to supply the stylopharyngeus muscles and the constrictors of the pharynx though these may well receive a motor supply from the vagus The sensory

Treatment of Facial nerve Lesions When the cause of the facial nerve lesion is known an attempt to remove it should be made There is no evidence that local treatment affects the course of Bell s palsy Massage and electrical stimulation to the affected muscles are often advised on theoretical grounds in the hope of minimizing the wasting but if the nerve recovers the muscles will soon regain their strength if it does not recover stimulating the muscles is futile Patients who are embarrassed by their facial asymmetry can be helped by an Allen Paul splint which consists of a hook of skin coloured plastic supporting the angle of the mouth and attached to a denture or tooth If the eye is never properly closed it may be necessary to wear goggles to protect the cornea

When the nerve has been damaged an end to end suture may be tried though this is usually not pos sible if the lesion is proximal to the stylomastoid foramen An attempt to graft either the 11th or 12th cranial nerves to the peripheral end of the facial nerve can then be tried This should be per formed as soon as possible when the nerve is cut in mastoid operations or in the removal of an acoustic neuroma In other types of peripheral facial paralysis it should be delayed for six months or more to determine whether spontaneous re generation will occur

Facial Spasm Clonic facial spasm may occur spontaneously or after partial regeneration of an injured facial nerve The spontaneous disorder is known as clonic facial hemispasm and is almost always associated with some minor impairment of the facial nerve which can be brought out by testing the facial movements Occasionally spasm is pro duced by a condition causing pressure on the facial nerve such as Paget s disease or an acoustic neuroma though more often no cause is found If the patient is very worried by the spasms the facial nerve may be partially sectioned or injected with alcohol This causes a facial paresis and on recovery the spasms occasionally do not return If they do return permanent relief can be obtained only by anastomosing the 7th nerve to the 11th or 12th nerves

Acoustic or 8th Nerve

The 8th nerve consists of two parts the cochlear nerve which is concerned with hearing and comes from the cochlea and the vestibular nerve which is concerned with postural and equilibratory func tions and comes from the semicircular canals the utricle and the saccule They run together to the brain stem and then separate to be distributed to entirely different central connexions

The Cochlear Nerve

Interruption of the cochlear fibres causes nerve or perception deafness This causes a loss more marked for high pitched tones In this type of deaf ness a vibrating tuning fork which should not be lower in pitch than 512 when applied to the vertex seems to be localized to the ear with the better hearing whereas in conduction (middle ear) deaf ness the opposite is the case Similarly in perception deafness air conduction is better than bone con duction whereas in conduction deafness the reverse is the case

Perception deafness may be produced by acute labyrinthitis and by toxic substances of which salicylates quinine and streptomycin are the com monest, and it also occurs in the ageing process The nerve may be damaged by injury neoplasms of the nerve itself or of associated neighbouring structures inflammations of the meninges and vas cular processes Within the brain stem tumours vascular lesions demyelinating processes and in flammations may damage the nucleus

Tinnitus Tinnitus is an hallucination of noise caused by abnormal excitation of the auditory apparatus or its afferent path Every variety of noise is described and it may be continuous inter mittent unilateral or bilateral When severe it may interfere with hearing though usually it is associated with deafness which is responsible for the hearing difficulty It is most obvious at night when other noises are not present to act as a distraction

There are many causes of tinnitus It may be associated with obstruction of the conducting apparatus such as wax in the external auditory meatus Eustachian obstruction and acute otitis media Alteration of circulation within the inner ear is a frequent cause and may be produced by generalized arteriosclerosis hypertension severe anaemia aortic incompetence and otosclerosis Drug induced tinnitus too may be of circulatory origin Sounds produced within the cranium as by a carotico cavernous aneurysm or a glomus jugulare tumour involving the petrous bone may be cor ducted to the ear and cause tinnitus Pressure of a tumour or local inflammation affecting the 8th nerve may also cause it Lesions of the central nervous system are a rare cause of tinnitus though it may occur in association with deafness after vascular or other lesions of the lateral part of the pons Irritative lesions of the auditory cortex give rise to a noise but this is usually too complex to be des cribed as tinnitus

Unfortunately tinnitus if at all persistent is often associated with depression particularly in the elderly and this may make recovery extremely slow

manipulating food and severe dysarthria Tremor of the tongue is present in general paralysis of the insane in chronic alcoholism and occasionally in Parkinsonism An apraxia of the tongue *i e* a difficulty in protruding it voluntarily often accompanies motor aphasia If however the tongue is protruded involuntarily as when licking the lips a full movement may occur

Peripheral Nerve Lesions

Traumatic Lesions

Following the experience gained in the last war three types of nerve injury are recognized Neurotmesis is complete anatomical division of the nerve Axonotmesis is a lesion in continuity in which true Wallerian degeneration occurs though the supporting structures of the nerve are not divided Neurapraxia is a condition of transient block with an incomplete defect in nerve function not associated with peripheral degeneration which usually recovers completely and relatively rapidly

Ischaemic lesions may involve motor and sensory nerves as well as muscles and they may result from arterial injury or occlusion (of which tourniquet paralysis is an example) Closed fractures may also produce ischaemic palsy Repeated or prolonged pressure on a nerve leads to ischaemia producing oedema extending above and below the source of pressure A neurapraxia first develops following presure but if this goes on axonotmesis may occur with fibrosis which prevents recovery

Complete division of a nerve results in a lower motor neurone paralysis of the innervated muscles Sensation is lost in the area of supply of the nerve but complete loss occurs only in the area exclusively supplied by the nerve and it is surrounded by a zone in which there is overlap and only partial loss of sensation. There are also vasomotor sudomotor and trophic changes The analgesic area of skin becomes dry and inelastic and ceases to sweat and it is bluer and colder than normal particularly in cold weather The limb may become oedematous if it hangs down The growth of nails is retarded and if the skin is injured it heals slowly

In neurapraxia the functions of the nerve are temporarily impaired There is very little muscular wasting though the loss of function is mainly motor and the electrical reactions of the muscles persist unchanged Subjective sensory disturbances are common though objective sensory disurbances are generally partial and often minimal postural sensibility being most affected Loss of sweating is unusual. Recovery is fairly rapid beginning after 2 or 3 weeks and usually being complete in 6 to 8 weeks

Causalgia

Causalgia is an extremely distressing symptom usually associated with incomplete lesions of the peripheral nerves and beginning a week or two after the injury It is most common following damage to the inner cord of the brachial plexus or the median or sciatic nerve Intense and persistent burning pain is felt often with paroxysmal exacerbations produced by contact. It may also be increased by *emotional reaction on the part of the patient* external noises vibration or even an overfull bladder The affected limb is pink and sweating the skin is tight and glossy and the nails are curved and tender and grow rapidly The finger pads are wasted and the nail beds may protrude The joints are stiff and swollen and the bones are rarefied and may be very brittle Tenderness may be produced by superficial or deep stimulation and this superficial tenderness extends over the whole of the cutaneous area innervated by the nerve and is much more extensive than the area of anaesthesia The nerve itself may be tender throughout the whole of its course but there may be very little associated muscular paralysis.

If the patient is seen early sedatives and analgesics should be given and the limb mobilized as far as the patient will allow However the most effective treatment is to block the sympathetic supply to the nerve with procaine If this gives relief but the pain later returns the sympathetic supply may be excised surgically If the symptoms have been present for a long time probably no treatment is effective

Lesions of the Brachial Plexus

Brachial plexus paralysis is rare and is almost always traumatic

Upper Plexus Paralysis (Erb-Duchenne Type)

This is due to a lesion of the branch from the 5th and sometimes the 6th cervical root It is the result of indirect violence the nerve being torn by a forcible increase in the angle between the head and shoulder It is the common form of birth injury and is produced by traction on the head when one shoulder lags behind In adults it may be due to a fall on the shoulder forcing the head to one side The resulting paralysis affects the deltoid biceps brachialis anterior supra and infraspinatus rhomboids and brachio radialis If the 6th-cervical root is affected there may be weakness also of the serratus anterior latissimus dorsi triceps upper part

fibres carry general sensation from the upper part of the pharynx and taste sensation from the posterior third of the tongue Isolated lesions of the peripheral part of the nerve or its nucleus are uncommon and usually produce no significant disability Taste may be lost on the posterior part of the tongue and the palatal reflex is absent on the side of the lesion If the 9th nerve is involved by inflammatory or neoplastic conditions as may happen at the jugular foramen the 10th and 11th nerves are usually involved as well

Glosso pharyngeal Neuralgia This is characterized by paroxysms of excruciating pain in the region of the tonsils and in the posterior pharynx the back of the tongue and deep in the ear In common with trigeminal neuralgia it usually has no apparent cause though it is occasionally due to an overlong styloid process or tumour in that region It is relatively rare its incidence being only about a twentieth of that of trigeminal neuralgia

The paroxysms of pain are burning or stabbing in character and are sharply localized to the back of the throat radiating into the ear They may occur spontaneously but more often are precipitated by swallowing talking or by pressure on the tonsils or posterior pharynx The attacks may last only a few seconds but may be prolonged and frequently repeated though long remissions are common Owing to the difficulty with swallowing patients tend to eat as little as possible and considerable loss of weight may occur

The diagnosis is established if pain can be precipitated by pressure in the tonsillar fossa The pain disappears if the affected area is painted with 5 to 10 per cent cocaine until it becomes anaesthetic

Treatment is by section of the 9th nerve This may be carried out by exposing the nerve in the tonsillar fossa and then avulsing it by cutting the nerve high up in the neck as it emerges from the jugular foramen or by cutting the nerve in its intracranial course The results are extremely satisfactory by any of these techniques if all the fibres of the nerves are cut

Vagus or 10th Nerve

The vagus nerve arises from the nucleus ambiguus and the dorsal motor nucleus both being situated in the medulla The former innervates the muscles of the palate pharynx and larynx the latter supplies the autonomic innervation of the heart lungs oesophagus stomach and small intestine

Unilateral lesions of the nucleus ambiguus produce dysarthria and dysphagia neither of very severe degree Some dissociation may occur the upper part of the nucleus producing dysarthria and the lower part dysphagia The difficulty in swallowing is usually slight and it can be seen that the palate on the affected side is relaxed and the uvula deviated to the opposite side on phonation The palatal reflex is absent on the affected side and a so called curtain movement of the pharynx can be seen the whole pharynx deviating laterally to the normal side on phonation

The nuclei of the 10th nerve may be damaged by inflammations particularly anterior poliomyelitis intra medullary tumours syringobulbia vascular lesions demyelinating disorders and degenerative processes such as amyotrophic lateral sclerosis The nerve itself or its branches may be involved in polyneuritis or compressed by tumours or aneurysms If the pharyngeal branches are injured there is difficulty in swallowing Lesions of the superior laryngeal nerve produce anaesthesia of the larynx and paralysis of the cricothyroid muscle and the voice is weak and tires readily The recurrent laryngeal nerve may be damaged by aneurysm of the aorta operations on the neck or the pressure of tumours with resultant hoarseness and dysphonia the vocal cords being paralysed in the cadaveric position Complete paralysis of both recurrent laryngeal nerves produces aphonia and inspiratory stridor Partial bilateral paralysis affects the abductors and causes severe dyspnoea and respiratory stridor without much alteration of the voice

Spinal Accessory or 11th Nerve

The spinal part of the 11th nerve innervates the sternomastoid and the trapezius muscles The accessory part of the nerve has its origin in the nucleus ambiguus and with the vagus innervates the pharynx and larynx Paralysis of the spinal portion causes weakness and wasting of the sternomastoid and trapezius muscles with consequent weakness of rotatory movements of the head to the opposite side and of shrugging of the shoulder The nucleus and the nerve may be affected by the same pathological processes as affect the vagus nerve

Hypoglossal or 12th Nerve

This nerve is motor to the muscles of the tongue its nucleus is in the medulla The nerve or nucleus may be injured by all the processes which affect the vagus nerve and nucleus Unilateral lesions produce atrophy and paralysis of the muscles of one half of the tongue and the protruded tongue is deviated towards the paralysed side Fasciculation of the muscles is seen in processes involving the nucleus such as amyotrophic lateral sclerosis and syringobulbia Bilateral lesions of the nucleus or nerve produce atrophy of both sides of the tongue and paralysis of all movements with difficulty in

of him Recovery may take up to two years and may even then be incomplete

The Circumflex Nerve

Damage to this nerve which can occur easily as it passes round the neck of the humerus causes paralysis and wasting of the deltoid muscle and teres minor and it is therefore not possible to elevate the arm more than a few degrees from the side There is usually an area of diminished sensibility on the lateral aspect of the upper arm

The Musculo-spiral (Radial) Nerve

This is easily damaged by direct trauma particularly as it runs round the humerus in the musculo spiral groove Occasionally it is affected by indirect trauma as by sudden contraction of the triceps the nerve being squeezed in the musculo spiral groove This results in weakness of the triceps the brachio radialis the extensors of the wrist fingers and thumb and the supinators Treatment is to splint the arm to prevent wrist and finger drop and perhaps to use elastic extension for the fingers The outlook is usually good

The Median Nerve

This supplies the pronators of the forearm the radial flexor of the wrist the superficial flexor of the fingers the flexors of the thumb and the lateral half (or occasionally the whole) of the deep flexor of the fingers Of the small muscles of the hand it supplies the abductor pollicis brevis the opponens pollicis part of the flexor brevis pollicis and usually the two radial lumbricales However the nerve supply of the small muscles of the hand varies considerably Although the sensory supply to the anterior aspect of the thumb the outer two and a half fingers and the corresponding part of the palm is provided wholly by the median nerve the degree of sensory impairment after median nerve lesions is variable and the affected area may be much smaller than this

The median nerve may be injured in any part of its course by direct trauma as by stabs or bullet wounds Continuous minor trauma may also affect the nerve in any part of its course particularly where it is passing over bones Occupational disorders producing lesions of the median nerve in the hand are not uncommon the symptoms then being confined entirely to the small muscles

Acroparaesthesia

This is a condition of burning paraesthesias usually occurring paroxysmally at night in the hands of middle aged women It may be unilateral or bilateral though the dominant limb is usually affected first and to a greater extent Associated with this there may be an area of numbness affecting the median supplied fingers Occasionally patients refer the symptoms to the whole hand not just to the median supplied area This appears to be due to their great unpleasantness and the feeling that they radiate which makes localization difficult Sometimes the symptoms stop at the wrist but in about 50 to 60 per cent of patients an aching pain is felt up the arm to the elbow and in a few even to the shoulder The symptoms are at their worst in the night preventing adequate sleep In the day they may be precipitated by specific manœuvres such as the wringing of washing polishing knitting sewing and writing

Any condition which narrows the carpal tunnel may produce the manifestations Fractures at the wrist or of the carpus especially if set in bad positions tenosynovitis and palmar ganglia may be found The symptoms most frequently arise spontaneously particularly at the menopause or during pregnancy There may be no abnormal physical signs but if the condition has been present for long a greater or less degree of wasting and weakness of the abductor pollicis brevis and some impairment of sensation over the terminal pads of the median fingers may be found The diagnosis may be confirmed by measuring the conduction time along the median nerve as it passes through the wrist and comparing that with the conduction time in the nerve at other levels Any delay in either motor or sensory fibres will confirm the diagnosis of median nerve compression

While some patients recover spontaneously and others recover on change of occupation or diminution of the amount of work a number do not improve at all and life may be made extremely miserable for them They are best treated by decompressing the median nerve in the carpal tunnel by section of the flexor retinaculum at the wrist and in the palm This operation gives immediate symptomatic relief if carried out adequately but marked sensory loss and marked wasting may take many months to recover

The Ulnar Nerve

This supplies the flexor carpi ulnaris and the inner half of the flexor profundus digitorum In the hand it usually supplies the muscles of the hypothenar eminence the inner two lumbricales the palmar and dorsal interossei the adductor of the thumb and inner head of the flexor brevis pollicis Any or all of these muscles may be affected by lesions of the ulnar nerve according to the level at which the lesion occurs The common site of

of pectorals and extensor carpi radialis The affected muscles are wasted and the resulting posture is characteristic the arm hanging to the side internally rotated at the shoulder with the elbow extended and the forearm pronated The biceps and supinator reflexes are lost Sensory loss may be absent but occasionally there is a small area of anaesthesia overlying the deltoid

Surgical intervention does not help The condition is best treated by putting the arm on an abduction splint with a movable joint at the elbow giving electrical stimulation to the affected muscles and encouraging the patient to exercise them as they recover The outlook is good particularly in the birth injuries

Lower Plexus Paralysis (Klumpke type)

This is produced by traction on the arm when it is abducted, the 1st dorsal root and sometimes the 8th cervical root being torn It may be due to birth injury or to falling and hanging on to something with the hand The paralysis and wasting involve the small muscles of the hand resulting in a typical claw hand If the 8th cervical root is affected there may be wasting and weakness of the ulnar flexors of wrist and fingers Sensory loss occurs along the ulnar border of the hand and slightly up the medial border of the forearm Occasionally the cervical sympathetic is also affected

Costoclavicular Syndrome

The branches of the brachial plexus and the vascular supply to the upper limb may be compressed as they pass from the neck into the axilla by both normal and abnormal structures These structures include a cervical rib bands of fibrous tissue running from the elongated transverse process of the 7th cervical vertebra to the 1st rib and if the outlet from the neck to the axilla is particularly oblique or narrow the normal 1st rib or scalenus anticus muscle Occasionally normal structures and their relations are altered in middle life by loss of tone in the muscles of the shoulder girdle or by traction due to carrying heavy weights and symptoms develop at that time

Clinical Picture The onset is usually gradual The symptoms may be sensory motor or vascular alone or in any combination Pain is the commonest sensory symptom and is usually referred to the ulnar border of the hand and forearm Tingling numbness or other paraesthesias are also common All these symptoms may be relieved by altering the position of the arm relative to the shoulder as by putting the hand above the head Sensory examination may reveal impairment of cutaneous sensibility in the little finger and on the ulnar border of the hand and it may extend for a short distance along the medial border of the forearm The small muscles of the hand are usually weak and wasted though not all may be affected equally Sometimes Horner s syndrome of cervical sympathetic paralysis is present Vascular symptoms consist of attacks of blanching or cyanosis of the fingers and occasionally the ischaemia is sufficiently severe to produce gangrene The peripheral pulses may be unequal in the two arms and the pulse may be affected by altering the position of the shoulder Occasionally a murmur can be heard in the subclavian artery as it passes over an abnormal rib and this murmur may be conducted up the vessels of the neck and may even be heard in the head Rarely an aneurysmal dilatation of the third part of the subclavian artery is formed with clot formation within the aneurysmal sac from which peripheral emboli are thrown off Sometimes the subclavian artery thromboses completely A cervical rib may be both visible and palpable in the neck

The only treatment which is of any value is surgical removal of the abnormality whether it be bony or fibrous If the symptoms are due to the abnormality rapid relief of the manifestations occurs though muscular wasting may be long in recovering It must be remembered that only 5 to 10 per cent of patients with cervical ribs have symptoms which are attributable to this abnormality At one time costoclavicular compression was regarded as the cause of acroparaesthesiae and many operations for enlarging the space were undertaken in the hope of relieving this condition with most disappointing results and the operation has tended therefore to fall into disrepute There can be no doubt however that there are a number of cases in which symptoms are produced by compression at this level and surgery here is of great value

The Long Thoracic Nerve

This nerve which innervates the serratus anterior may be injured by direct trauma or by carrying weights on the shoulder More frequently it is the site of a neuritis of the shoulder girdle type (neuralgic amyotrophy) Initially this is associated with considerable pain in the neck and after a few days the nerve ceases to function and the serratus anterior is paralysed This muscle fixes the scapula to the chest wall when forward pressure is exerted with the upper limb Paralysis causes no deformity of the scapula at rest but on elevating the arm forward particularly against resistance the inner border of the scapula becomes winged and the patient is unable to raise the limb above the head in front

severe pain The tendon reflexes are diminished in the affected segment Sensory loss is rare though there may be paraesthesias in the fingers Complete recovery may occur after a few weeks or the patient may have a series of subacute exacerbations of brachial neuralgia with long intervening periods of aching in the neck and shoulder girdle muscles

In the exacerbations stiff neck usually develops as in the acute episodes and this is followed by a march of the pain down the limb the outer aspect of the shoulder the postero lateral aspect of the upper arm and the dorsum of the forearm being affected There may also be typical root pains brought on by coughing and straining or putting the head towards the side of the lesion and paraes thesias usually in the tip of the index or index and middle fingers The affected muscles are weak These are the triceps and extensors of wrist and fingers if the 7th cervical root is mainly affected and the biceps and brachialis anterior if the 6th cervical root is affected The corresponding reflexes are diminished or absent Sensory loss is difficult to find The other cervical roots are rarely involved

Plain X rays may demonstrate narrowing of inter vertebral discs with osteophytosis but this is a common finding in any patient who is reaching middle age even when there are no symptoms

Treatment Immobilization either in bed or by wearing some form of collar gives considerable relief Intermittent or continuous gentle traction by a head halter can be helpful but manipulation may carry some risk of spinal cord damage if there is much central protrusion of the intervertebral discs Adequate analgesics should be used to obtain re laxation If the attack has been severe the patient may need to wear a collar of plastic material leather or sorbo rubber to prevent movements of the neck With such conservative treatment most episodes come to an end in 4–8 weeks

Lumbar Disc Lesions and Sciatica

Lumbar disc protrusion may be produced by trauma lifting heavy weights or falling with the back flexed in the forward position being usual This trauma is often superimposed upon the de generative changes which occur especially in older people but also in the young Protrusions between the 4th and 5th lumbar or the 5th lumbar and 1st sacral vertebrae are the most common and may again be central postero lateral or lateral

Sciatica is frequently preceded by lumbar pain for many years though occasionally it follows the first attack of lumbago The lumbago itself is often acute with fixation of the back but soon either clears or becomes subacute After a few days pain radiates down the back of the leg from the buttock to the ankle The pain is deep and gnawing and on it is superimposed flashes of root pain produced by coughing sneezing or straining The pain is intensified by stooping which may be difficult and it interferes with sleep There may be a positive feeling of numbness or heaviness in the foot Examination frequently shows loss of the normal lumbar lordosis which may even be turned into a kyphosis Forward flexion of the spine is limited and there is often spasm of the back muscles There is flabbiness and slight wasting of the muscles (in cluding the glutei) supplied by the affected root Compression of the 1st sacral root causes weakness of the small muscles of the foot and the calf muscles and the ankle jerk is diminished or lost Compression of the 5th lumbar root causes weak ness of the peronei and sometimes complete foot drop with no change in the ankle jerk but some times a slight increase in the knee jerk If the 4th lumbar root is affected there is weakness and wast ing of the quadriceps with absence or diminution of the knee jerk The plantar reflexes are always flexor Mild sensory loss may occur according to the root which is involved but this is rare The patient stands in a characteristic posture with the back slightly bent and the lumbar spine flexed usually towards the affected side The hip is slightly flexed and internally rotated and the knee is slightly flexed the weight being taken on the sound limb

X rays may show no change whatsoever or some narrowing of the intervertebral space They should however always be taken to exclude other bony disorders

In mild cases the severe pain may last only 2 or 3 weeks and in a month or so the patient may make a complete recovery experiencing only minor ach ing or cramp in the affected muscles for a short time and some pain precipitated by stooping Occa sionally the condition becomes subacute or chronic and pain of greater or lesser degree may persist for up to many months Recovery ultimately occurs but there may be some residual disability in the back with difficulty in bending and some numbness in the outer border of the foot or in one of the toes Relapses are not uncommon and are usually pro duced by some inadvertent movement or slight injury

Treatment The vast majority of patients with intervertebral disc sciatica recover completely with conservative treatment This consists of rest in bed on a firm mattress with sufficient analgesics to control the pain If the pain is extremely severe morphia may be necessary If greater immobiliza tion is necessary a plaster jacket with a spica on the affected lower limb may be applied After the

damage is where the nerve passes through the bony groove behind the internal epicondyle of the elbow Here it is at its most superficial and lies against bone and is traumatized by the flexion and extension of the elbow This is more likely to happen if there has been a fracture at the elbow which increases the normal carrying angle A pressure neuritis occurs and the nerve may be swollen at this point by a traumatic neurofibroma The symptoms are pain and paraesthesias particularly in the little finger and the inner aspect of the hand with weakness and wasting of the muscles innervated below the elbow Occasionally the ulnar nerve is damaged by some occupation which causes constant pressure on the palm Then only the small muscles of the hand may be affected and there is usually no sensory loss as the superficial or sensory branch of the ulnar nerve is given off at the wrist

Treatment of the pressure neuritis at the elbow is to transpose the nerve to the front of the elbow Rapid recovery usually occurs unless muscle wasting is profound and of long duration

Nerves of the Lower Limb

Lateral Cutaneous Nerve of the Thigh

This enters the thigh below the lateral part of the inguinal ligament and then pierces the deep fascia running obliquely Pressure on the nerve occurs whenever the tension of the deep fascia of the thigh is increased thus narrowing the oblique tunnel through which it runs This may be produced by changes in posture or by increase in size of the abdomen particularly by obesity Direct pressure as by a belt or corset may also compress the nerve The symptoms are characteristic and have been given the name meralgia paraesthetica Pain numbness and paraesthesias occur usually in the lateral aspect of the middle or lower thigh The symptoms may be brought on by walking and then the suspicion of vascular disease in the limb may arise There may be slight diminution of sensation in the affected region If the symptoms are very troublesome even after the patient has been reassured as to their relative insignificance relief may be given by exposing the nerve as it passes through the deep fascia If a neurofibroma is present avulsion of the nerve is to be preferred

The Femoral Nerve

This may be affected by a psoas abscess by neoplasms within the pelvis or by trauma to the pelvis or femur Weakness of the quadriceps and an absent knee jerk are present Sensory loss varies but may involve the front of the shin

The Sciatic Nerve

This too may be damaged by fractures of the pelvis and femur and by direct trauma or compressed within the pelvis by neoplasms Weakness or paralysis of the muscles supplied by the nerve follow These conditions however are relatively rare

The lateral popliteal nerve is commonly affected particularly as it winds round the head of the fibula Here it may be compressed by keeping the legs crossed for too long by direct trauma or by fractures of the head of the fibula Great weakness of dorsiflexion and eversion of the foot and toes results Inversion also is weakened and there is sensory loss over the dorsal aspect of the foot

The medial popliteal nerve is rarely affected

Treatment of these lesions of the sciatic nerve or its major branches necessitates the prevention of foot drop both by day and by night Recovery is relatively slow both in the major nerve and its branches

INTERVERTEBRAL DISC DISEASE

Degenerative changes of the intervertebral discs are the commonest cause of root compression They are due to increasing age and repeated minor trauma and occur mainly in the cervical and lumbar regions being rare in the dorsal region Degeneration of the disc may produce a small round protrusion almost like a neoplasm or a generalized bulge of the whole disc A mainly posterior or postero lateral protrusion presses on the spinal cord or cauda equina a lateral protrusion bulges into the intervertebral foramen and compresses a nerve root

Brachial Neuralgia (Acute Protrusions)

There is often but not always a history of stiff necks in the past lasting for a few days at a time Following some minor trauma or occasionally spontaneously the patient suddenly has excruciating pain in his neck with limitation of movement Both active and passive movements intensify the pain This is referred along the course of the affected root and the muscles supplied become flabby and may even waste a little Some muscular weakness is present but is difficult to assess because of the

6 Rarities such as the so-called progressive hypertrophic polyneuritis and the polyneuritis associated with sarcoidosis

Acute Toxic Polyneuritis (Guillain Barré)

This condition frequently begins with an initial febrile illness which may settle down and after a day or two paralysis appears The first symptoms may be very slight but if they are more marked they include headache vomiting slight pyrexia pains in the back and limbs and a feeling of stiffness in the neck and back After the latent period the paralytic symptoms come on very suddenly accompanied by further headache and perhaps a recurrence of pyrexia but slower progression may be found The paralysis may affect all four limbs simultaneously or may begin in the lower limbs and spread to the upper All the muscles of the limb are commonly affected the difference between the peripheral and proximal muscles being slight In severe cases the neck and trunk may also be involved and frequently the facial muscles on both sides are paralysed The bulbar muscles may be involved with resultant dysphagia from pharyngeal paralysis The muscles of respiration are affected frequently External ophthalmoplegia is rare Paralysed muscles are flaccid and often tender but not greatly wasted unless the condition lasts for a long time The superficial and deep reflexes are diminished or lost There may be spontaneous pain numbnes and tingling in the limbs All forms of sensation are impaired over the peripheral segments of the limbs The sphincters are rarely affected Cerebral symptoms are usually absent and consciousness is unclouded until the end though a confusional state may develop General symptoms may include albuminuria and an erythematous rash There is a moderate polymorphonuclear leucocytosis The cerebro spinal fluid shows a great excess of protein with normal or only slightly increased mononuclear cells

The mortality rate used to be high death being due to paralysis of the respiratory muscles The disorder may fluctuate and after an apparent improvement a fatal relapse may follow Severely paralysed patients can now be kept alive but their recovery may be incomplete Even the mild cases rarely recover in less than 3 months and the moderate cases in less than 6 to 9 months

Treatment An important part of treatment is good nursing Bulbar and respiratory paralysis are treated exactly as in poliomyelitis Cortisone is very helpful in most cases Doses in the order of 200 or 300 mg (or the equivalent in its derivatives) should be given for 2 3 or 4 days the dose being then gradually reduced Good position of the muscles must be maintained and as soon as possible passive and active movements instituted

Alcoholic Polyneuritis

This form of polyneuritis is probably due to a deficiency in vitamin B_1 (aneurin) alcoholism leading to a deficiency of intake of food and with it that of vitamins Unfortunately when the condition has progressed to any considerable degree the administration of aneurin may not give a complete recovery because of the permanent changes which have taken place

Clinical Picture Sensory symptoms are prominent the patient complaining of numbness tingling paraesthesias and sometimes severe and burning pain in the hands and feet Cramps in the calves also occur particularly in the night Following the sensory disturbances the limbs become weak the lower limbs being more affected than the upper and the peripheral parts more than the proximal In severe cases foot drop and wrist drop may be present with wasting of the peripheral muscles of all four limbs Owing to sensory loss particularly deep sensation ataxia may be conspicuous and there is blunting of all forms of sensibility in the periphery of the limbs with cutaneous anaesthesia and analgesia usually extending up to the elbow and knees The muscles of the calves are particularly tender but the appreciation of pain may be delayed Tendon reflexes are diminished or lost the peripheral reflexes disappearing before the proximal The skin of the extremities is often oedematous and sweating Contractures are readily produced particularly in the flexors of the fingers and in the ham strings There is usually no sphincter disturbance and abnormalities of the cranial nerves are uncommon Korsakow s syndrome (loss of memory with confabulation) or an alcoholic dementia may occur The cerebro spinal fluid is usually normal but occasionally a considerable rise in protein is found

The outlook depends upon the stage at which treatment begins If large doses of Vitamin B_1 balanced by the other members of the B complex are administered early considerable recovery may take place but in long standing cases this is always incomplete

Treatment Complete rest is essential and large doses of the Vitamin B complex are given probably parenterally at first This must include 50–100 mg of aneurin daily and a good mixed diet should be given Alcohol should be withdrawn if the patient will tolerate this

pain has gone which may take several weeks gradual activity is introduced and the patient slowly assumes the upright position He may be helped by a firm corset with shaped paravertebral metal bars or alternatively an ambulant plaster jacket These supports may have to be worn for several months Very chronic cases are occasionally helped by an epidural injection of 20 ml of 1 per cent procaine solution followed by 80 to 100 ml of normal saline through the sacro coccygeal foramina

If there is no response to conservative treatment the affected disc may be removed surgically by laminectomy It is important that adequate rehabilitation follow the operation otherwise the recovery will not be as impressive as it should

Differential Diagnosis of Root Compression The commonest causes of compression of both cervical and lumbar roots are a prolapsed intervertebral disc or an osteophyte in the foramen of exit All the other causes which are similar in both the cervical and lumbar region are relatively rare Within the spinal canal the nerve roots may be compressed by tumours of the spinal cord or of neighbouring nerve roots or may be the site of inflammation due to syphilis The nerves may be compressed within the vertebral foramina by disease of the vertebral column or they may be involved by inflammations usually chronic of the membranes A vertebral collapse may be caused by tuberculosis or other forms of chronic osteitis primary or secondary neoplasm or trauma In the lumbar region subluxation (spondylolisthesis) or other abnormalities of the 5th lumbar vertebra may compress the lumbo sacral cauda equina The lumbo sacral plexus may also suffer from tuberculosis of the sacro iliac joint from compression by secondary carcinoma of the internal iliac glands or from involvement in a psoas abscess Within the pelvis compression may arise from a neoplasm from the pregnant uterus or from the foetal head during delivery Within the buttock the sciatic nerve is subject to various forms of trauma and may be the site of tumours such as neurofibroma sarcoma or angioma In the cervical region neoplasms and inflamed glands in the neck may cause much the same manifestations as a root compression It is doubtful whether true interstitial neuritis of the sciatic or femoral nerve or of the nerves leading into the arm occurs

Diagnosis may be helped by straight X ray This may show changes in the intervertebral disc region or probably more important lesions of the vertebral column of other origin Lumbar puncture may or may not show an abnormality of the cerebro spinal fluid depending upon the size of the herniation of the intervertebral disc Finally myelography may establish the diagnosis beyond doubt

POLYNEURITIS

Polyneuritis manifests itself by the simultaneous impairment of function of many peripheral nerves The distal parts are affected much more than the proximal there being a gentle march up the limbs The lower limbs are affected more than the upper limbs The disorder may affect the cranial nerves and is occasionally restricted to them There is usually symmetrical flaccid muscular weakness and sensory disturbances again more marked in the periphery than in the proximal segments

Aetiology There are very many causes of polyneuritis which may be classified as follows

1 Toxins from without Most metals particularly the heavy metals may cause polyneuritis Arsenic and mercury are most often responsible others are antimony copper bismuth and lead though lead has other ill effects as well as causing polyneuritis Non metallic substances include phosphorus carbon monoxide carbon disulphide sulphonamides dinitrobenzole and orthotricresyl phosphate (apiol and ginger palsy)

2 Deficiency and metabolic disorders Examples are beriberi chronic alcoholism pellagra pernicious anaemia subacute combined degeneration haematoporphyrinuria diabetes myxoedema acromegaly and amyloid disease In addition deficiency states may be secondary to other diseases and particularly to diseases of the gastro intestinal tract such as sprue coeliac disease gastro colic fistula and the surgical removal of long lengths of small intestine

3 Hypersensitivity phenomena such as acute toxic or febrile polyneuritis and rheumatic polyneuritis (Mononeuritis multiplex due to multiple vascular lesions as in polyarteritis nodosa may mimic polyneuritis)

4 *Acute and chronic infections* Septicaemia typhoid and paratyphoid fevers scarlet fever influenza tuberculosis mumps typhus malaria and measles are all very rarely complicated by polyneuritis

5 Bacterial toxins especially dipththeria tetanus and botulism

6 Rarities such as the so called progressive hypertrophic polyneuritis and the polyneuritis associated with sarcoidosis

Acute Toxic Polyneuritis (Guillain Barré)

This condition frequently begins with an initial febrile illness which may settle down and after a day or two paralysis appears The first symptoms may be very slight but if they are more marked they include headache vomiting slight pyrexia pains in the back and limbs and a feeling of stiffness in the neck and back After the latent period the paralytic symptoms come on very suddenly accompanied by further headache and perhaps a recurrence of pyrexia but slower progression may be found The paralysis may affect all four limbs simultaneously or may begin in the lower limbs and spread to the upper All the muscles of the limb are commonly affected the difference between the peripheral and proximal muscles being slight In severe cases the neck and trunk may also be involved and frequently the facial muscles on both sides are paralysed The bulbar muscles may be involved with resultant dysphagia from pharyngeal paralysis The muscles of respiration are affected frequently External ophthalmoplegia is rare Paralysed muscles are flaccid and often tender but not greatly wasted unless the condition lasts for a long time The superficial and deep reflexes are diminished or lost There may be spontaneous pain numbness and tingling in the limbs All forms of sensation are impaired over the peripheral segments of the limbs The sphincters are rarely affected Cerebral symptoms are usually absent and consciousness is unclouded until the end though a confusional state may develop General symptoms may include albuminuria and an erythematous rash There is a moderate polymorphonuclear leucocytosis The cerebro spinal fluid shows a great excess of protein with normal or only slightly increased mononuclear cells

The mortality rate used to be high death being due to paralysis of the respiratory muscles The disorder may fluctuate and after an apparent improvement a fatal relapse may follow Severely paralysed patients can now be kept alive but their recovery may be incomplete Even the mild cases rarely recover in less than 3 months and the moderate cases in less than 6 to 9 months

Treatment An important part of treatment is good nursing Bulbar and respiratory paralysis are treated exactly as in poliomyelitis Cortisone is very helpful in most cases Doses in the order of 200 or 300 mg (or the equivalent in its derivatives) should be given for 2 3 or 4 days the dose being then gradually reduced Good position of the muscles must be maintained and as soon as possible passive and active movements instituted

Alcoholic Polyneuritis

This form of polyneuritis is probably due to a deficiency in vitamin B_1 (aneurin) alcoholism leading to a deficiency of intake of food and with it that of vitamins Unfortunately when the condition has progressed to any considerable degree the administration of aneurin may not give a complete recovery because of the permanent changes which have taken place

Clinical Picture Sensory symptoms are prominent the patient complaining of numbness tingling paraesthesias and sometimes severe and burning pain in the hands and feet Cramps in the calves also occur particularly in the night Following the sensory disturbances the limbs become weak the lower limbs being more affected than the upper and the peripheral parts more than the proximal In severe cases foot drop and wrist drop may be present with wasting of the peripheral muscles of all four limbs Owing to sensory loss particularly deep sensation ataxia may be conspicuous and there is blunting of all forms of sensibility in the periphery of the limbs with cutaneous anaesthesia and analgesia usually extending up to the elbow and knees The muscles of the calves are particularly tender but the appreciation of pain may be delayed Tendon reflexes are diminished or lost the peripheral reflexes disappearing before the proximal The skin of the extremities is often oedematous and sweating Contractures are readily produced particularly in the flexors of the fingers and in the ham strings There is usually no sphincter disturbance and abnormalities of the cranial nerves are uncommon Korsakow s syndrome (loss of memory with confabulation) or an alcoholic dementia may occur The cerebro spinal fluid is usually normal but occasionally a considerable rise in protein is found

The outlook depends upon the stage at which treatment begins If large doses of Vitamin B_1 balanced by the other members of the B complex are administered early considerable recovery may take place but in long standing cases this is always incomplete

Treatment Complete rest is essential and large doses of the Vitamin B complex are given probably parenterally at first This must include 50–100 mg of aneurin daily and a good mixed diet should be given Alcohol should be withdrawn if the patient will tolerate this

Localized Neuritis of the Shoulder girdle (Neuralgic Amyotrophy)

This condition may arise spontaneously or may be a hyper sensitivity reaction to the administration of anti toxin or anti serum When it arises spontaneously pain in the root of the neck which is *often severe is the first manifestation and it is fol*lowed after a few days by weakness and wasting of some of the shoulder girdle muscles Most commonly the serratus anterior the spinati the deltoid and the trapezius and sometimes the biceps and brachialis are affected More rarely lower fibres of the brachial plexus are affected with weakness in the triceps brachioradialis and even extensors of the fingers There may be some sensory loss though this is not so common as the motor involvement The lesions may be bilateral No changes are usually found in the cerebro spinal fluid The condition is very chronic and recovery takes many months or even up to a year or two and may even then be incomplete

When neuralgic amyotrophy is a hypersensitivity reaction it usually occurs about ten days after the administration of a serum or anti toxin Most commonly the 5th and 6th cervical roots are affected much more rarely the 7th root is involved Pain may be quite profound and muscular weakness and wasting of the muscles supplied by the affected roots is severe Sensory loss may be present but is not usually so marked as motor involvement No treatment is very effective but cortisone or its derivatives given as soon as the condition declares itself are probably helpful

Tumours of the Brain

One seventh of all malignant neoplasms in man are cerebral tumours and they cause 1 per cent of *all deaths*

Aetiology and Pathology The aetiology of nearly all cerebral tumours is unknown Occasionally a meningioma develops at the site of a previous head injury and in a few cases congenital abnormality plays a part particularly in the formation of the angiomatous tumours or angioblastomas and in tumours of the craniopharyngeal pouch Tumours may occur at any age but different types of tumours have a definite age incidence which will be referred to under their own headings

The gliomas form about 41 per cent of all intracranial tumours the meningiomas 13 per cent auditory nerve tumours 10 per cent secondary carcinoma about 5 per cent cranio pharyngiomas 7 per cent and pituitary adenomas about 5 per cent

Gliomas

Gliomas are derived from the cells which constitute the supporting tissue of the nervous system They are variously classified according to the particular stage of development of the tumour cells though a single glioma may contain many different types of cell Most gliomas are infiltrative tumours and they may grow round areas of nervous tissue leaving them relatively intact The tumour may be much more extensive therefore than would be supposed from the physical signs Most gliomas are either astrocytomas which are relatively slowly growing or glioblastomas which are rapidly growing Medulloblastomas are particularly found in children They arise in the region of the roof of the 4th ventricle and have a marked tendency to become disseminated through the subarachnoid space in the brain and spinal cord *They are particularly* malignant but highly radio sensitive when treated for the first or second time Glioblastomas are extremely malignant usually arise in middle life and occur mainly in the cerebral hemispheres They infiltrate the brain extensively and may reach an enormous size No form of treatment prolongs life for more than a few months to a year

Astrocytomas are infiltrating growths occurring at any age in the cerebral hemispheres or in the cerebellum They grow slowly are relatively benign and patients may survive for many years from the time they begin and even after the diagnosis is established Cystic formation within the tumour is not uncommon

Meningiomas

These were thought to arise from the dura mater but are now believed to arise from the arachnoid cells which penetrate the dura to form the arachnoid villi projecting into the dural venous sinuses Usually they are single large and irregularly lobulated but occasionally form a flat plaque spreading over the inner surface of the dura Frequently they produce a hyperostosis in the overlying bone but occasionally tend to invade the bone with which they are in contact This may be absorbed and then new bone is laid down over the tumour *so as to* form a bony mass Meningiomas do not invade the brain but compress it and as they are slowly growing the disturbance of cerebral function may be quite small As they arise from the arachnoid villi

they are most frequently found along the course of the large intracranial venous sinuses particularly the superior longitudinal sinus (parasagittal meningiomas) the sphenoparietal sinus and the middle meningeal veins (meningiomas of the convexity) They may also arise from the sinuses of the olfactory groove the ethmoids and those around the sella turcica Meningiomas are rare below the tentorium but may develop from the sinuses of the tentorium itself

Auditory Nerve Tumours

These are usually unilateral When bilateral they are frequently associated with generalized neurofibromatosis and may also be associated with multiple meningiomas and gliomas Similar tumours may occur though much more rarely on other cranial nerves such as the trigeminal and upon the spinal roots and peripheral nerves

Blood vessel Tumours

1 *Angiomatous Malformations* These may be telangiectases or capillary angiomas and are occasionally associated with hereditary telangiectasia More frequently they are arteriovenous malformations consisting of a mass of enlarged tortuous vessels supplied by large arteries (usually from one but occasionally both hemispheres) and fed also from the tentorium and drained by several large veins Increasing use of arteriography has shown these malformations to be much more common than was thought

2 *Haemangiomablastomas* These are tumours composed of angioblasts which are primitive cells forming the foetal blood vessels They have a marked tendency to form cysts containing xanthochromic fluid in nerve tissues The tumour may exist as a small nodule in the wall of the cyst. They are invariably subtentorial and are frequently associated with abnormalities in other parts of the body such as angioblastoma of the retina (von Hippel s disease) and similar conditions in the spinal cord pancreas and kidneys and with hypernephromas of the kidneys and suprarenal glands When many such abnormalities exist the condition is probably familial

Metastatic Tumours

Rather less than one tenth of cerebral tumours are secondary to a primary growth elsewhere This is most frequently in the lung but may be in the breast prostate pancreas or kidney Occasionally a secondary tumour in the brain is the first intimation of a growth Metastases are usually multiple and rapidly growing and the history is correspondingly short

Clinical Picture of Cerebral Tumours

The manifestations of an intracranial tumour are usually divided into two groups The general symptoms and signs which are related to a raised intracranial pressure may be produced by any tumour the special symptoms and signs depend upon the location as well as the nature of the tumour

General Symptoms and Signs

These may be completely absent even with a greatly raised intracranial pressure or they may be present indicating raised intracranial pressure when no focal signs can be found

Headache This is the most common manifestation though it frequently cannot be differentiated either by its nature or location from other causes of headache Sometimes the pain is localized but more frequently it is generalized or more intense in the frontal or occipital regions The headache is most frequently felt on the same side as the tumour Localized tenderness of the scalp or the underlying skull is not absolutely localizing but is most commonly present in close relationship to the tumour The headache is usually intermittent quite irregular and lasts for minutes or hours It is almost always increased by change of posture coughing or straining Its cause is uncertain and is not directly related to the level of intracranial pressure The present view is that the pain is probably produced by pressure or traction on the pain producing structures such as dura blood vessels or nerves

Nausea and Vomiting These are much less frequent than headache Projectile vomiting is not uncommon and is usually not preceded by nausea or headache

Papilloedema Swelling of the optic nerve head with engorgement of the retinal veins and haemorrhages into the nerve and adjacent retina is commonly found with intracranial tumours but the absence of papilloedema does not necessarily mean that the intracranial pressure is not raised In general choked discs or papilloedema appear early in all patients with intracranial tumours whatever their nature if they are so located as to interfere with the circulation of the cerebro spinal fluid and thus produce an internal hydrocephalus

It should be possible to differentiate with certainty between the choked disc of intracranial tumour and the swelling of the nerve head such as occurs in multiple sclerosis or other demyelinating disorders or arterial diseases of the retina In choked disc the swelling of the nerve head is usually greater than in optic neuritis retrobulbar neuritis or multiple sclerosis The haemorrhages in the retina seem to confine the swelling to the nerve head or

adjacent retina Visual acuity is normal in the early stages of a choked disc but there is an *enlargement of the blind spot* proportional to the degree of swelling of the nerve head When swelling of the optic disc persists for more than many weeks or months a secondary type of atrophy develops in *the optic nerve* The peripheral fields are constricted and there is a gradual failure of central vision which may progress to complete blindness

Convulsions The local or generalized seizures of brain tumours do not differ in any way from those which occur with other organic lesions of the brain Attacks of loss of consciousness are commonly the first symptoms of an intracranial tumour and the diagnosis must be considered in all patients with seizures beginning after the second or third decade

Mental Symptoms The mental symptoms of intra cranial tumours include lethargy drowsiness changes in personality disorders of conduct im pairment of mental faculties and psychotic episodes These may occur in any intracranial tumour but are more likely when the lesion is situated in the anterior part of the cerebral hemispheres The patient may void his bladder or rectum with com plete indifference to his situation this behaviour being usually due to an indifference to the pro priety of these acts rather than to true incontinence This is usually associated with a tumour in the frontal lobe

False Localizing Signs When the intracranial pressure is very high these may be produced by distortion of the intracranial structures Unilateral or bilateral weakness of the external rectus muscle is common and hemiplegia due to distortion of the brain stem with pressure against the edge of the tentorium may occur Similarly the posterior cere bral artery may be compressed causing a misleading homonymous hemianopia When the brain begins to herniate through the *tentorium changes due to* ocular motor paralysis together with fixed dilated pupils may be present The dilated 3rd ventricle may through the supraoptic recess press on the optic chiasm and produce a bitemporal hemianopia and even pituitary insufficiency

Focal Symptoms and Signs

Frontal Lobe Tumours in the pre frontal region are often very difficult to localize Those in the minor hemisphere may cause no symptoms until *late in* their course Headache may be an early *symptom* but evidence of raised intracranial pres *sure is* usually late and may be absent throughout *Mental symptoms* may occur early particularly if *the corpus* callosum is involved A frontal situation *is particularly* likely if mental symptoms develop before signs of raised intracranial pressure There is usually a progressive dementia which shows itself *as a defective grasp of* the situation and a failure of the thought processes The intellect may deteriorate still more seriously and insight may be completely lost The patient becomes careless of dress and appearance and of sphincter control The bladder and bowels may be emptied anywhere with no sense of propriety He may be jocular and facetious making very simple jokes or puns repeatedly or bad tempered irritable and depressed

Generalized convulsions occur in about half the cases If the tumour is situated near the base the aura may be associated with speech—usually with *a desire to speak without being able to do so*—and there may be a sensation of the throat being gripped If the tumour is in the upper aspect of the lobe adversive attacks with turning of the head and eyes to the opposite side and clonic and tonic movements of the contralateral limbs are common The patient may be aware that the eyes and head are being turned but is unable to prevent this hap pening Catatonia may occur the patient being im mobile in one attitude for a long time

Expressive aphasia may occur when the inferior frontal convolution is affected A grasp reflex is not infrequently present in the opposite hand but may be found only in the foot Occasionally the *grasp reflex is associated* with tonic innervation that is an inability to relax after contraction If the tumour extends backwards the pyramidal fibres are compressed leading to weakness on the opposite side of the body usually most in the face and tongue Tremor may be present on the same or opposite side Pressure on the olfactory nerve which lies on the floor of the anterior fossa and on the inferior surface of the frontal lobe causes unilateral anosmia This is not infrequent in meningiomas which arise from the olfactory groove and if th *tumour extends backwards it* may compress the optic nerve causing primary optic atrophy on the side of the lesion while giving rise to a generalized rise of intracranial pressure producing papilloed ma in the opposite eye

A tumour in the pre central zone may cause the symptoms of pyramidal deficiency very early These may be associated with focal convulsions which may affect the whole of the opposite side or *only* a part of it if they are limited there *is usually no* loss of consciousness Sometimes *a fo al* convulsion continues for hours or days (*epilepsia partialis con tinua*) Motor weakness due to *destruction of the* pyramidal fibres is *most frequently a monoplegia* though even in the affected limb parts may *escape* The usual reflex changes associated *with pyra* midal lesions are found A tumour of *the falx par* ticularly in the region of *the paracentral lobule*

may produce weakness of both lower limbs beginning in the feet but frequently asymmetrical There may be retention of urine and when the tumour extends backwards impairment of postural sensibility in the toes Focal convulsions are usually associated with some weakness of the part of the body which is the focus of the fit but after each convulsion there is often a temporary extension of the weakness to other parts

Temporal Lobe Temporal lobe tumours may give very few signs and symptoms particularly when in the minor hemisphere However if the uncinate gyrus is involved the so-called uncinate attacks are produced These are characterized by (1) an olfactory or gustatory aura which consists of a hallucination of taste or smell This is usually unpleasant and the patient may have great difficulty in describing it. There may also be a curious taste referred to the nasopharynx (2) There may be an abnormal state of consciousness in which the patient feels dazed or appears dreamy as though in a trance having usually stopped what he is doing and remaining absolutely still Falling is rare There may be no recollection of this or the patient may describe feeling as though everything that is happening has happened before and that he is re living part of his life This feeling of familiarity the déjà vu phenomenon may be of a stereotyped experience (3) Occasionally motor phenomena occur These are usually smacking lips involuntary licking of the lips or tasting and chewing movements

Psychomotor attacks as described under epilepsy may be associated with uncinate attacks or may appear quite separately Visual field defects are present in about half the cases of temporal lobe tumours and are due to involvement of the lower fibres of the optic radiation as they pass round the tip of the temporal horn of the ventricle The defect is therefore a crossed upper quadrant anopia Visual hallucinations which are usually rather complex and well formed with images of events or happenings may be present There may be tinnitus or auditory hallucinations in which the patient hears certain stereotyped phrases and though he may not remember them for what they are in each attack he recognizes that they are familiar A lesion in the dominant temporal lobe may produce some form of aphasia In mild cases this may be merely a nominal dysphasia but if it is more severe the patient may be unable to understand spoken words or even written words It may go on to a jargon aphasia Apraxia is much rarer As the tumour enlarges neighbourhood symptoms due to affection of the pyramidal tract are produced there being a hemiparesis with particular weakness of the face

Parietal Lobe Sensory disturbances are the characteristic feature of parietal lobe tumours Irritation of the post-central convolution causes sensory focal attacks consisting of paraesthesias such as tingling or electric shocks Pain is unusual. Paraesthesias begin either in the corner of the mouth or a finger or toe and spread to involve other parts of the body They may occur alone or be followed by a similarly spreading motor attack Destructive lesions of the post-central convolution cause sensory loss of the so-called cortical type that is discriminative aspects of sensation particularly postural sensibility and tactile discrimination are lost Crude appreciation of pain and temperature may be left intact Occasionally there is disturbance of the memory of sensory impressions so that the patient is unable to recognize objects placed in the affected hand This is called astereognosis and it is sometimes present when no other sensory involvement can be detected Deep seated tumours reaching the thalamus may produce a thalamic over reaction that is an exaggerated response to unpleasant stimuli on the opposite side of the body occasionally associated with spontaneous unpleasant pain in the same region As the fibres of the optic radiation pass deeply through the parietal lobe a crossed homonymous defect of visual fields is not uncommon Tumours of the posterior part of the parietal lobe produce higher sensory defects with disturbances of the body image there being unawareness of parts of the body on the opposite side and unawareness of parts of the surrounding space The patient with a right hemisphere defect may continuously ignore the left half of space and when finding his way about may turn continuously to the right thus losing himself in his own home or in the hospital ward A dominant hemisphere defect may produce alexia and agraphia

Occipital Lobe Posterior tumours usually cause headache early and frequently cause epilepsy The fits are often preceded by an unformed visual aura such as flashes of light moving from one side towards the middle line If the lesion is fairly far forward in the occipital lobe the attack may begin with a turning of the eyes towards the opposite side This may be followed by the head and even by the whole trunk The patient usually says that something has appeared in his field of vision which he is trying to follow and which constantly moves away from him Frequently there is a crossed homonymous hemianopia extending up to the fixation point

Corpus Callosum Mental symptoms such as apathy drowsiness and defect of memory are the most prominent manifestations of tumours of the corpus callosum Generalized convulsions are often present. If the tumour extends laterally into the

white matter damage to the pyramidal tract which is usually symmetrical may occur early When anteriorly placed there is a grasp reflex on one or both sides Tremor and choreiform movements due to involvement of the basal ganglia may occur

Third Ventricle The 3rd ventricle may be occupied by a colloid cyst or may be invaded by a tumour arising below or above or in the basal ganglia When the 3rd ventricle is invaded the tumour has usually given rise to signs due to its primary situation Diagnosis may, however be difficult when there is a colloid cyst The symptoms may be those of an acute or intermittent hydrocephalus with severe paroxysmal headache influenced by changes in the position of the head Papilloedema may be the only symptom but not infrequently a progressive dementia probably produced by a chronic hydrocephalus is present

Brain Stem Tumours arising in the mid brain may cause internal hydrocephalus fairly early due to obstruction of the aqueduct of Sylvius However the commonest tumour is a slowly growing infiltrating glioma which may go on for years without obstructing the aqueduct and without producing acute symptoms of hydrocephalus Ocular abnormalities are prominent with paresis of conjugate ocular deviation either upwards or laterally lid retraction or ptosis and paresis of convergence The pupils may be unequal and are often dilated and the pupillary reflexes may be abnormal Some involvement of the pyramidal tracts is common particularly in the later stages and tonic fits characterized by opisthotonos with extension of all four limbs and loss of consciousness may occur Tremor is common and nystagmus and ataxia are produced by damage to the cerebellar peduncles Involvement of the sensory pathways produces extensive areas of analgesia and defect of postural sensibility A tumour lower down in the pons and medulla causes early weakness of the external rectus on one or both sides and there may be weakness in the bulbar supplied muscles and impairment of sensation in the trigeminal distribution Nystagmus and ataxia are common in the lower tumours even though the cerebellum is not affected

Pineal Body Tumours of the pineal produce signs of raised intracranial pressure due to compression of the upper part of the aqueduct of Sylvius There are early signs of pressure on the dorsal aspect of the mid brain as shown by diminution of conjugate ocular movement upwards with retraction or ptosis of the upper lids and inequality of the pupils which are usually dilated Later there may be bilateral pyramidal signs In young boys a syndrome consisting of mental precocity abnormal growth of the skeleton and premature development of the genitalia and secondary sexual characteristics occurs occasionally

Optic Chiasm In this region several possible masses may be present (1) Tumours of the pituitary (2) Tumours of the hypophysial duct (3) Suprasellar meningiomas (4) Gliomas of the optic chiasm (5) Centrally placed aneurysms

Pituitary Tumours Adenomas of the pituitary gland form approximately 15 per cent of intracranial tumours There are three types the chromophobe the chromophil or acidophil and the basophil. The chromophobe adenoma is 3 or 4 times as common as the acidophil and the basophil is relatively rare Mixed types may occur Basophil adenomas are usually very small They do not enlarge the sella turcica and never extend out of it to compress the neighbouring structures They are associated with symptoms of endocrine dysfunction (Cushing s syndrome) Both chromophobe and acidophil adenomas enlarge the sella turcica and may break out of it to compress the optic chiasm and neighbouring parts of the cerebral hemispheres Rarely they grow forward or extend backwards along the brain stem into the posterior fossa The manifestations of pituitary tumours are therefore local due to pressure on the optic chiasm and neighbouring structures and endocrine due to pressure on the remaining portion of the gland or to disturbances of hormone production The endocrine manifestations are considered on p 118

Chromophobe Adenoma The early symptoms may be headache often frontal or bitemporal and thought to be due to pressure of the tumour on the diaphragm of the sella and on the sella itself Once the tumour extends out of the sella pressure on the optic chiasm may be present The visual field defect is variable but most commonly the posterior part of the optic chiasm is affected This usually produces at first a defect in the upper temporal field which gradually enlarges to become a complete bitemporal hemianopia If central vision is involved the visual acuity is also diminished Frequently however the visual field defect is asymmetrical Complete blindness in one eye may be associated with loss of the temporal field of vision in the other or there may be a homonymous hemianopia with or without a defect in the temporal field of the side opposite to the hemianopia Later the optic discs may become atrophic As the defect of the visual fields progresses signs of pituitary deficiency occur Extension of the growth may interfere with the pathway to the supraoptic nucleus producing diabetes insipidus Extension into the 3rd ventricle causes increased intracranial pressure though if the optic discs are atrophic papilloedema rarely develops

Involvement of the cerebral peduncles produces pyramidal signs usually very asymmetrical and extension into the temporal lobe produces convulsive seizures with a temporal lobe type of aura

Acidophil Adenomas Pressure symptoms and signs are much less frequent than in the chromophobe type and a tumour may be present for very many years without producing anything other than endocrine changes The endocrine symptoms are usually regarded as an exaggeration of the normal function of the anterior lobe of the pituitary that is pathological hyperpituitrism A tumour arising before growth has ceased causes gigantism (p 118) in adult life it causes acromegaly (p 119) When the tumour breaks out of the sella the pressure effects are the same as in chromophobe adenomas

Hypophysial Tumours or Craniopharyngiomas These tumours arise within embryonic rests from the craniopharyngeal pouch which goes to the development of the hypophysial stalk Symptoms therefore usually appear early Approximately a third of the cases are seen before the age of 15 They usually arise above the diaphragm of the sella very rarely they develop within the sella itself Because of their situation between the floor of the 3rd ventricle and the pituitary and their occurrence at an early age they produce a large variety of disturbances of growth and metabolism depending in which direction they enlarge Pressure may occur either on the pituitary or the hypothalamus or on both these structures Patients may show extreme degrees of adiposity emaciation polyuria or the reverse dwarfism sexual infantilism or premature physical senility

The pressure symptoms are more conspicuous than those of pituitary tumours In childhood the skull may be enlarged and the sutures separated Headache and vomiting may be severe and papilloedema is perhaps commoner than optic atrophy The tumour compresses the optic nerves chiasm or tracts leading to field defects characteristic of the part of the visual pathway involved As the optic chiasm is compressed from above a bitemporal hemianopia beginning in the lower quadrants usually results The tumour may extend into the frontal or temporal lobes or backwards along the base of the brain into the posterior fossa compressing the cerebral peduncles and the cranial nerves as it does so

Suprasellar Meningiomas These occur in adult life The principal symptoms are visual due to compression of the optic nerve chiasm or tract Primary optic atrophy is the rule and a variety of visual field defects may be produced One eye is affected much before the other The tumours frequently grow up into the temporal lobe leading to uncinate fits or general convulsions and hemiparesis

Cerebellum The cerebellum is a common site of tumour particularly in childhood The usual tumour is a medulloblastoma which occurs in the first ten years of life It usually arises in the midline from the roof of the 4th ventricle Astrocytomas and glioblastomas in childhood are also most common in the cerebellum and both are often cystic Many tuberculomas are found in the cerebellum

Often cerebellar tumours arise in the midline and extend into one or both lateral lobes particularly in children In adults lateral lobe tumours are not so uncommon

Midline cerebellar tumours usually give a short history with symptoms of increased intracranial pressure Headache vomiting and papilloedema are all well marked In children hydrocephalus often leads to enlargement of the skull with separation of sutures and some symptoms of pituitary insufficiency Cerebellar deficiency is usually seen in the difficulties with equilibrium either in standing or walking There may be little or no ataxia of the upper limbs or on formal testing of the lower limbs if the patient is lying down The patient often complains of giddiness though there may be no true vertigo and tends to fall backwards or occasionally forwards The gait is ataxic especially on turns Nystagmus is absent but there is some asymmetrical muscular hypotonia Compression of the mid brain may lead to tonic fits as mentioned earlier The cranial nerves are often little affected except that the pupils may be dilated and react sluggishly to light Weakness of one or both external recti may be present when there is much rise of intracranial pressure There is little weakness of the limbs but an extensor plantar response may be found on one or both sides

When the tumour begins in the lateral lobe signs of increased intracranial pressure also appear early as a rule Suboccipital headache is common with some slight stiffness of the neck the muscles on the side of the tumour having the greatest degree of tone Clumsiness of the ipsilateral hand and a tendency to stagger to the side of the lesion and giddiness on shaking or turning the head are common Nystagmus is marked and most evident on conjugate deviation of the eyes to the side of the lesion The quick phase is usually directed towards the side of the lesion the slow recovery phase is directed to the middle line Occasionally the nystagmus is rotary The limbs on the side of the lesion are usually hypotonic the outstretched upper limb tending to sway and fall away if unsupported Ataxia is present on the affected side being greater in the upper limb on carrying out fine repetitive

movements *The gait is unsteady* the patient walks on a wide base deviating to the affected side and is liable to fall to that side when standing with the feet together and the eyes closed *Rapidly alternating* movements carried out with the affected limb are irregular jerky and arrhythmical The shoulder on the affected side is often at a lower level than the normal shoulder and the head is frequently rotated so that the occiput is directed towards the shoulder on the affected side Speech may be only slightly disturbed Neighbourhood symptoms are frequent the forward pressure by the tumour producing a dysfunction of the 5th to 12th cranial nerves on the same side the 5th 6th and 7th being most often affected Pressure upon the pons and medulla may lead to some signs of pyramidal defect on the opposite side of the body, and even occasionally to some sensory loss

Cerebellar Pontine Angle The commonest tumour in the cerebellar pontine angle is a tumour of the 8th nerve (an acoustic neuroma) These may be unilateral or bilateral in which case they are usually part of a generalized neurofibromatosis The tumours grow slowly and symptoms and signs may be present for years before there is any rise of intracranial pressure The first symptoms are usually due to disturbance of the function of the 8th nerve giving tinnitus followed by progressive deafness Rarely labyrinthine symptoms such as giddiness precede disturbance of hearing Headache is usually occipital or suboccipital and tends to begin just behind the mastoid of the affected region It may radiate to the frontal region In later stages the headache is generalized and there may be attacks of severe occipital pain radiating down the spine with retraction of the head and neck and some loss of function of medullary centres Papilloedema and vomiting develop late Paraesthesias which may be painful are occasionally felt in the face on the side of the lesion and attacks of facial spasm may occur Dysphagia is usually late

Examination shows great reduction of hearing and loss of responses to the caloric tests of labyrinthine function on the affected side There is some facial weakness on the affected side and some sensory loss in the trigeminal distribution usually shown first by diminution or loss of the corneal reflex The external rectus may be affected but the remaining cranial nerves are usually spared *Compression of the cerebellar hemisphere* causes symptoms of cerebellar deficiency on the side of the tumour Occasionally the brain stem is compressed, producing some hemiparesis and hemi anaesthesia X rays may show erosion of the petrous portion of the temporal bone particularly the internal auditory meatus

Other masses in the cerebellar pontine angle are meningiomas secondary deposits cholesteatomas and aneurysms of the basilar artery

Investigations

X rays Every case of suspected cerebral tumour *must have* a *straight* X ray of the chest because a high percentage of intracranial tumours are metastatic One of the commonest primaries is carcinoma of the bronchus which may be shown in an X ray though it has been completely unsuspected X rays of the skull are essential These may show raised intracranial pressure changes causing thinning of the dorsum sellae and enlargement of the sella turcica In children separation of the sutures and occasionally bulging of the anterior or middle fossa may be seen There may also be localized absorption of bone due to pressure of a neighbouring neoplasm This is particularly well seen in the sella turcica in pituitary tumours and in the internal auditory meatus in tumours of the auditory nerve A calcified pineal gland is occasionally seen displaced to one or other side and so helps in the lateralization of the tumour Many tumours including angiomas gliomas meningiomas and especially craniopharyngiomas may be calcified and visible on X rays

Pituitary tumours whether eosinophilic or chromophobe produce enlargement of the sella turcica This is ballooned and eroded and may extend downwards into the sphenoidal air sinus Craniopharyngiomas produce the general signs of increased intracranial pressure on X ray together with erosion of the clinoid processes and flattening of the sella turcica as the result of downward pressure by the tumour X ray evidence of calcification within the tumour is present in three quarters of the cases Suprasellar meningiomas rarely produce X ray changes though occasionally calcification occurs In glioma of the optic chiasm X ray usually shows enlargement of the sella turcica forwards and sometimes of the optic foramen *Aneurysms cannot be differentiated* unless they leak or rupture or have calcified walls visible as a ring in the X ray Angiography however will establish the diagnosis

Electroencephalography This investigation is useful as it may show the distortion of the normal rhythms and abnormal waves produced by oedema or some other disturbance of the cortex due to th tumour Occasionally the area is definitely located by a phase reversal in the wave forms on either side of the focus The neoplasm sometimes produces an

epileptogenic focus which may cause it to be suspected Progressive changes are particularly important as they strongly indicate a neoplasm

Cerebro-spinal Fluid Examination Lumbar puncture must be carried out with care If raised intracranial pressure is suspected only the smallest quantity of fluid should be removed The danger is that the removal of cerebro spinal fluid in the presence of raised intracranial pressure may produce coning through the tentorium or the foramen magnum

The pressure of the fluid as registered by a manometer may or may not be raised The protein content is often increased Occasionally a rais d cell count is found particularly if the tumour is close to the ventricular system and is rapidly growing or has undergone necrosis or is the site of a haemorrhage

Encephalography and Ventriculography The introduction of air into the subarachnoid space by lumbar puncture is encephalography its introduction into the ventricles through a brain needle is ventriculography If there is evidence of considerable rise of intracranial pressure ventriculography is the only safe procedure Changes in the size and position of the ventricular system and the sub arachnoid cisterns may be seen if they are adequately filled with air making it possible to localize the tumour However a small or infiltrating neoplasm may cause the manifestations of a tumour without producing any convincing changes in the ventricular system or sub arachnoid spaces

Angiography This is carried out by introducing radio opaque dyes into the cerebral circulation either through the carotid arteries or the vertebral arteries This technique is not entirely free from danger it may cause considerable swelling in a very vascular tumour may precipitate a fatal rise in intracranial pressure or may produce a permanent hemiplegia Distortion or displacement of the vessels can be seen in serial X rays while the dye is being introduced Occasionally new vessels can be visualized in meningiomas and angiomas Aneurysms which may have been mimicking a tumour can also be seen

Diagnosis

The most important aid to diagnosis is a full and accurate history The possibility of cerebral tumour should always be borne in mind whenever focal neurological symptoms develop slowly and gradually An acute symptomatology is unusual and most brain tumours are not associated with pyrexia or other signs of an infection

The common differential diagnosis is from the following conditions cerebro vascular accidents epilepsy (idiopathic or due to other causes) demyelinating diseases degenerative diseases and sub dural haematomas

Cerebro vascular Accidents These are most frequently of relatively sudden onset and except in the short time after the onset are rarely progressive the usual course being—if the patient survives—a steady though limited improvement In carotid ischaemia due to stenosis however there is occasionally a slowly advancing hemiplegia which may well mimic a neoplasm during the progressive stage Hypertension or arteriosclerosis do not necessarily favour cerebro vascular accidents rather than tumours as either may occur in the presence or absence of these vascular changes Occasionally an intracerebral haematoma suggests a neoplasm but once again the onset is sudden and the progression thereafter is relatively slow In any event surgical exploration is the correct treatment in this type of case

Infections of the nervous system are rarely confused with brain tumours unless they are very chronic or produce localized granulomas or abscesses since there is usually some general evidence of an infection Sarcoidosis a tuberculoma or —very much more rarely—a gumma occasionally cause difficulties in diagnosis

Demyelinating Diseases Multiple sclerosis is rarely confused with a neoplasm In Schilder s disease the signs and symptoms are occasionally progressive and localized to one region of the cortex or brain stem and a full investigation may be necessary to establish the diagnosis

Epilepsy This may be a manifestation of a tumour at any age but as brain lesions occurring after the first month or two of life never produce true or classical petit mal this type of epilepsy is not therefore evidence of an intracranial tumour Tumours may grow so slowly that convulsive seizures may be the only manifestation for a great number of years Oligodendrogliomas may be present for 10 or 15 years with epilepsy as the only manifestation Tumour should always be suspected if attacks develop in adult life or if they are focal

Degenerative Diseases Pre senile dementia is the degenerative disease most likely to be confused with a cerebral neoplasm particularly if it is associated with convulsions However signs of rising intra cranial pressure never develop

Subdural haematomas may suggest tumour particularly when the causative head injury was very mild or has been forgotten or the patient is a chronic alcoholic Investigation and exploration are frequently necessary to make the differential diagnosis

Treatment

The best treatment of an intracranial tumour is to remove it but this must not be carried out at the expense of removal of or damage to a great deal of normal cerebral tissue When there is evidence of a great rise of intracranial pressure and time is needed for diagnosis and to tide the patient over dehydration is of value One of the best methods of lowering intracranial pressure is a rectal injection of 200 ml (8 oz) of a 25 per cent solution of magnesium sulphate The patient should retain it if possible for half an hour A more rapid reduction of intracranial pressure is achieved by injecting a hypertonic solution such as 100 ml of 50 per cent sucrose solution very slowly intravenously Magnesium sulphate by mouth and restricting the fluid intake also cause some dehydration

If an inoperable tumour is obstructing the flow of cerebro spinal fluid it may be possible to carry out the short circuiting operation devised by Torkildsen This consists of putting a polythene tube from the occipital horn of the lateral ventricles into the cisterna magna

X ray treatment may retard the growth of pituitary adenomas and relieve the headache if this is due to pressure on the sella turcica by the tumour It should never be used when the tumour is producing raised intracranial pressure or visual defect. Surgery then is certainly the treatment of choice Irradiation is particularly useful in some gliomas The medulloblastomas are the most radio sensitive and may regress for several years though with further irradiation they become less and less sensitive There may be a temporary regression of some glioblastomas but the dose of radiation necessary for this purpose is usually so large that there is a danger of radio necrosis of normal cerebral tissue In metastatic deposits due to a radio sensitive primary such as carcinoma of the breast X ray therapy may be very useful indeed for the relief of focal epilepsy or of focal signs such as hemiplegia hemianaesthesia and aphasia It may also be extremely helpful in posterior fossa deposits which are producing intense headaches and vomiting Each patient with metastases from carcinoma of the bronchus must be considered on his merits as only some of these metastases are radio sensitive and it would be unjustified to add the distress of deep X rays to that of the primary condition

Spinal Tumours

Spinal tumours are less common than intracranial tumours in the ratio of one to four but are similar in nature and origin They may arise from the parenchyma of the cord its roots the meningeal coverings the intraspinal vascular network or the vertebral column They may also be metastases from tumours elsewhere in the body The tumours are divided into the two large groups of intramedullary and extramedullary Two thirds of all primary spinal tumours are the benign encapsulated meningiomas and neurofibromas The incidence in the two sexes is approximately equal with the exception of the meningiomas which are more common in women Spinal tumours are more common in the thoracic region but in relation to the actual length of the various portions of the cord the distribution is approximately equal

Extramedullary Tumours These are usually limited to several segments of the spinal cord and usually produce signs and symptoms of a partial or complete transverse lesion of the cord The first symptoms are pains and paraesthesias due to compression of the nerve roots followed by sensory deficit weakness and muscular wasting in the distribution of the affected roots The early signs of cord compression are a spastic weakness of the muscles and impairment of cutaneous and proprioceptive sensation below the level of the lesion impairment of control of the bladder and to a lesser extent of the rectum and increase of the tendon reflexes with extensor plantar responses and loss of the appropriate abdominal responses There is considerable variation in the severity and distribution of the weakness and sensory loss depending on the location of the tumour in relation to anterior lateral or posterior part of the spinal cord Severe compression of the cord is followed by necrosis with destruction of grey and white matter and may produce the signs of a complete or almost complete transection of the cord There is usually wasting and atrophy of the muscles at the level of the lesion and below the level of the lesion there is a paraplegia in flexion complete loss of all forms of sensation loss of the appropriate abdominal responses and a mass reflex If the symptoms of a transverse cord lesion come on rapidly the tumour has probably occluded the spinal vessels the transverse lesion being really of vascular origin

Intramedullary Tumours Only one tenth of all spinal tumours are intramedullary The signs they produce are usually indistinguishable from those of

the extramedullary tumours though the root manifestations are less common If the tumour extends over several segments in addition to the evidence of cord compression there are signs of funicular lesion as shown by muscles wasting loss of reflexes and occasionally dissociated sensory loss extending over several dermatomes The saddle area is usually spared when general hypaesthesia and hypalgesia are present and the sphincters may be affected later than in the extramedullary tumours

Affection of the conus medullaris and cauda equina by tumour produces pain in the back or in the lower extremities often mimicking sciatica Bladder symptoms and impotence develop early and as the tumour extends there is a flaccid paralysis of the lower extremities atrophy of the leg muscles and foot drop Fasciculation of muscles may be seen and sensory loss is usually present in the lower lumbar and sacral dermatomes This may be slight or may be very severe indeed involving the saddle area and producing trophic ulcers

Investigations Straight X rays may show localized destruction of the vertebral processes changes in the contour or increased separation of the pedicles Distortion of the paraspinal tissues may be seen if the tumour extends through the intervertebral foramen (the dumb bell tumour of a neurofibroma) There may also be proliferation of bone and some calcification

A complete or incomplete block in the circulation of the cerebro spinal fluid in the subarachnoid space may be demonstrated by lumbar puncture A needle is inserted in the subarachnoid space fairly low down the jugular veins are compressed and only a small rise or no rise of cerebro spinal fluid pressure results Small tumours may not show much abnormality by this test (Queckenstedt s Test) Complete block usually gives a yellowish fluid with a protein content as high as 100 to 1 000 mg per cent Sugar and chloride content are normal

Myelography by the introduction of a radio opaque oil into the subarachnoid space frequently localizes the level of the lesion in the spinal canal

Differential Diagnosis Spinal tumours must be differentiated from other conditions producing progressive disease of the spinal cord These include syphilis multiple sclerosis syringomyelia subacute combined degeneration of the cord amyotrophic lateral sclerosis and anomalies of the cervical spine and base of the skull Arachnoiditis and radiculitis may require to be differentiated Ruptured intervertebral discs may produce a local extramedullary compression or diffuse compression of the cervical cord can occur in cervical spondylosis

Treatment The treatment of spinal tumours is either their removal by surgery or by X ray irradiation Surgery is most helpful whenever there are signs of spinal compression and if the lesion is dealt with early enough a complete restoration of function may occur

Developmental Defects

Many defects of the brain or spinal cord which may be limited to the nervous system or include bone skin and subcutaneous tissue may be present at birth The causes of the maldevelopments are not known Genetic factors play some part because the defects are occasionally familial but other causes are probably more frequent The central nervous system when developing is especially susceptible to anoxia irradiation and certain infectious diseases in the mother such as German measles It has also been suggested that some of these lesions may be due to an endocrine disturbance as cortisone during the early stages of pregnancy may produce failure in development

Congenital Hydrocephalus

The term hydrocephalus is used to describe many conditions in which there is an excess of fluid in the cranial cavity but is usually applied to the presence of excess fluid under increased pressure It may develop in infants or adults as the result of occlusion of the cerebro spinal fluid pathways by tumours of the 3rd ventricle brain stem or posterior fossa Developmental hydrocephalus is due to an obstruction to the normal flow of cerebro spinal fluid by a failure of development of the brain or as the result of intrauterine infections of the nervous system This form of hydrocephalus may be communicating or non communicating depending on whether there is free communication between the fluid in the ventricles and in the lumbar sub arachnoid space This can be shown by the recovery from the lumbar fluid of a dye injected into the cerebral ventricles In non communicating hydrocephalus the obstruction to the flow of fluid is either in the aqueduct of Sylvius or in the 4th ventricle In communicating hydrocephalus the fluid escapes from the 4th ventricle but remains confined to the basal cisterns

Pathogenesis and Pathology Passage of fluid from the 3rd to 4th ventricle may be prevented by many

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Degenerative and Heredo-degenerative Diseases

Disorders of Lipoid Metabolism

A number of diseases associated with disturbance in lipoid metabolism involve the central nervous system All are rare but probably the most important is *cerebromacular degeneration or amaurotic* family idiocy This condition is characterized by progressive loss of vision dementia and paralysis It may occur in an infantile or a juvenile form and is inherited as a Mendelian recessive

Clinical Picture *Infantile Form* The infant develops normally until the third to sixth month of life when weakness of the neck trunk and extremity muscles becomes apparent He cannot sit up or lift his head from the bed has difficulty in turning over and drops objects The weakness increases in severity in the next few months until there is generalized paralysis At the same time there is loss of vision progressing to complete blindness The eyes are held wide open and there are rolling or roving movements of the eyeballs The pupils are dilated and do not react to light Ophthalmoscopic examination shows atrophy of the optic nerve and an oval or circular patch of greyish white atrophy of the macula with a cherry red spot in the centre of the atrophic area

Deafness may occur but more commonly the hearing is well preserved Myoclonic jerks and atypical convulsive seizures are common

Juvenile Form The symptoms begin any time between 4 and 18 years of age Loss of vision may develop from 1 to 3 years before the other symptoms These include generalized convulsions progressive paralysis and mental deterioration There may also be cerebellar ataxia and Parkinsonian rigidity The visual loss is due to optic atrophy and *macular degeneration but there is no cherry red* spot The disease progresses steadily but much more slowly than the infantile form and 10 to 15 years may elapse before death results This is usually due to intercurrent infection or status epilepticus

The cerebro spinal fluid blood and urine are all normal

The diagnosis is relatively easy in the infantile form the cherry red spot being pathognomonic It is much more difficult however in the juvenile forms where there may be atypical syndromes and no cherry red spot

There is no specific treatment Members of an afflicted family should probably be advised not to have children

Tuberous Sclerosis

This condition is characterized by the development fairly early in life of congenital tumours or malformations of the nervous system skin and sometimes other organs The prominent clinical features are facial naevi (adenoma sebaceum) recurrent convulsive seizures and retardation of mental development

Pre senile Dementia

Two diseases of unknown aetiology called Pick s and Alzheimer s disease are often familial and affect females much more frequently than males though isolated cases also occur The age of onset is between 40 and 65 years and the major symptoms of both conditions are progressive dementia and disturbances of speech The dementia is evident in dulling of intellectual faculties with slowing of thought and defective memory and increasing difficulty in living a normal life Disturbances of speech are perhaps out of proportion to the other disorders of intellect The cases usually fall into two groups in one apathy mutism and immobility are the most prominent features in the other restlessness and hyperactivity are present In both types however as the condition progresses dementia becomes profound and the patient becomes mute and *vegetative and rapidly ages in appearance About* 10 per cent of patients have convulsions

Though Pick s and Alzheimer s disease have different pathological appearances clinically they are identical In both the course is progressive terminating in complete incapacity and death and the duration varies from 4 to 10 years There is no effective treatment and institutional care is necessary

DISORDERS OF BASAL GANGLIA

Sydenham s Chorea

Aetiology and Pathology There is a close relationship between *chorea and rheumatic fever* (p 507) Approximately three quarters of the cases of chorea show other manifestations of rheumatic disease in the form of acute arthritis myocarditis *endocarditis or pericarditis The pathological* changes in the nervous system are not certainly

lesions The aqueduct of Sylvius may be absent but is more commonly narrowed by an overgrowth of ependymal cells Occasionally the aqueduct is obstructed by a thin membrane and outflow from the 4th ventricle may be made difficult by the absence or incomplete formation of the foramina of Magendie and Lushka Rarely these exits are obstructed by meningeal adhesions secondary to intrauterine meningitis Probably the most common cause of congenital hydrocephalus is the developmental abnormality named after Arnold Chiari in which part of the cerebellum and lower brain stem are invaginated through the foramen magnum into the upper part of the cervical canal

Congenital hydrocephalus is relatively rare In the usual case there is a progressive enlargement of the head in the first few months of life The cranial bones are thinned the sutures widened and the fontanelles bulge The roof of the orbit is depressed with downward and outward protrusion of the eye balls Papilloedema is rare because the head can expand Optic atrophy deafness spastic weakness of legs or arms and cerebellar ataxia are the commoner neurological symptoms Mental development is usually retarded the infant being slow in learning to walk and talk X rays show uniform enlargement of the head thinning of the calvarium and convolutional markings of the skull bones The cerebro spinal fluid pressure is increased

Patients with congenital hydrocephalus usually go progressively downhill and die in the first or second year from intercurrent infections

Treatment of congenital hydrocephalus is surgical Very many operations have been devised for relief of the condition but their value is uncertain Those which include excision or coagulation of the choroid plexus at the appropriate point and the production of a shunt from one of the ventricles into the subarachnoid space may be of some benefit The children need a great deal of rehabilitation of very graduated type both before and after operation

Spina Bifida

Spina bifida is a failure in the closure of the spinal column due to a defect in the development of vertebrae It is often associated with defects in the development of the spinal cord brain stem cerebellum or cerebrum or with meningocoeles meningomyelocoeles congenital tumours hydrocephalus or developmental defects in other parts of the body

Spina bifida may be present without any neurological symptoms If there are symptoms they are related to the extent of the defect in the nervous system and the presence or absence of tumour growths such as lipomas and dermoids With a lesion in the lumbar or sacral segments there is a disturbance in gait and impairment of control of sphincters Maldevelopment of the feet with various deformities usually unilateral and scoliosis are also common Frequently the defect in the spine can be detected by palpation and is evident by the presence of a localized overgrowth of hair or a hard lump in the skin at the site of the defect

Simple meningoceles may occur without any symptoms but when parts of the spinal cord are present in the sac some disability must occur

X rays often show the defect in the spine but cannot be proof that the symptoms are due to the radiological lesion

Treatment is by surgery where possible

Cerebral Palsy

Cerebral palsy is not a disease but a term used to describe a group of cases with damage to the nervous system in utero at birth or early in life

Pathology At one time it was thought that most cases were due to injury to the nervous system at birth but other factors account for the great majority of cases

Clinical Picture This is variable The cases can be divided into groups according to whether the main damage is in the motor cortex the basal ganglia or the cerebellum producing a spastic athetoid or ataxic picture There may also be mixed lesions Intellectual defect is not uncommon and there may be focal disorders such as aphasia apraxia and dysarthria If the brain damage is severe it may be obvious at birth but often it is shown later by feeding difficulties poverty of movements listlessness and lack of development of the ordinary hygienic habits

Course This varies widely Symptoms are usually most marked about the ages of 2 to 3 After this there may be some improvement as the patient learns to compensate for his disability

Treatment is by intensive physiotherapy and special education Orthopaedic surgery for the correction of deformities of the extremities is often very useful in the rehabilitation of the child Remarkable results can be obtained by an enthusiastic physiotherapist who spends a lot of time on one patient

Mendelian dominant Both sexes are affected and either sex may transmit the disease The symptoms may begin at any age though most commonly be tween 30 and 50 years

Clinical Picture The usual onset is the appear ance of abnormal movements though occasionally psychotic episodes or mental deterioration precede the movements by several years The movements are abrupt and jerky but less so than in Sydenham s or juvenile chorea Any muscles may be involved but the proximal girdle muscles and the trunk muscles are quite commonly affected When moderately advanced the movements are gross and caricature dancing whereas in the early stages there may be nothing beyond a simple restlessness or fidgetiness with slight grimacing and shrugging of the shoulders Abnormal movements are increased by emotional stimuli diminish when the patient is relaxed and disappear entirely during sleep In the early stages it may be possible to compensate for the abnormal movements but this becomes more and more difficult as they increase and speech usually becomes almost unintelligible Sensation and re flexes are not affected The mental symptoms are similar to those of any organic deterioration There are changes in personality impulsive behaviour and progressive memory defect and intellectual impairment Irritability forgetfulness lack of con centration apathy bouts of depression and fits of violence occur As the condition progresses the patient becomes slovenly incapable of dressing or feeding himself dirty incontinent and finally help less Convulsions are rare

Investigations Blood urine and cerebro spinal fluid are within normal limits The E E G shows a non specific diffuse abnormality Air encepha lography shows enlargement of the ventricles

Course This is chronically progressive and leads inevitably to death The average duration of life is 15 years from the onset though it varies widely

Treatment does not influence the course of the disease but sedation may reduce the severity of the movements Chlorpromazine (Largactil) has this effect and may make the patient a little more com fortable Recent reports suggest that procaine amide (Pronestyl) also reduces the movements

Paralysis Agitans (Parkinsonism)

Paralysis agitans or Parkinsonism may occur spontaneously or may be due to obvious disease of the nervous system The cases may be divided into three major groups spontaneous or idiopathic Parkinsonism symptomatic Parkinsonism and post encephalitic Parkinsonism

Idiopathic Parkinsonism The pathological find ings are degenerative changes in the basal nuclei and substantia nigra There may also be very slight loss of cells in the cerebral cortex The pathogenesis is unknown

Symptomatic Parkinsonism The disorder may follow injury to the nervous system by trauma or by carbon monoxide manganese and occasionally other metallic poisonings or may be due to cerebral arteriosclerosis Very rarely it is associated with a tumour Obviously the pathological findings vary but usually diffuse degenerative changes are found and cysts in the caudate and lenticular nuclei may be present particularly after carbon monoxide poisoning Small foci of softening of the basal ganglia may be found when cerebral arteriosclerosis is responsible and similar foci may be scattered throughout the brain

Post encephalitic Parkinsonism This term is used when the symptoms develop coincidental with or follow (after an interval of up to many years) an encephalitis of the lethargic (von Economo) type Degenerative changes are found in the basal nuclei particularly the substantia nigra with degeneration and calcification in the smaller vessels Perivascular lymphocytes are inconstant

Incidence Parkinsonism is quite common At present most cases belong to the so-called idiopathic group and the arteriosclerotic cases are the next most frequent. Post encephalitic Parkinsonism used to occur at all ages but is now rare because the causative encephalitis is almost extinct

Clinical Picture Tremor and rigidity are the basic abnormalities and give rise to the majority of symptoms These are usually of insidious onset and may be present for a long time before the patient becomes aware of them Usually the rigidity causes the condition to be noticed though occasionally tremor is the primary manifestation Rigidity shows itself as a slowing of the ability to perform usual activities and a feeling of stiffness and minor diffuse pain in the muscles Only one extremity may be affected at the beginning but in time it usually spreads to the other limb on the same side and then to the opposite side The pupils are usually normal but the eye movements may be jerky and limited in range Impairment of convergence is common Facial expression is fixed as a result of the rigidity of the muscles giving the mask like facies Volun tary and emotional movements of the face are slow and of limited range Occasionally a smile covering and illuminating the whole face breaks through but then tends to remain longer than usual Involuntary blinking of the eyelids is considerably decreased and a characteristic staring expression may be present On closing the eyes gently however a rapid movement of the eyelids—the so-called blepharo clonus—may develop Speech is frequently mildly

known because uncomplicated acute chorea is rarely fatal Degenerative changes in the nerve cells of the cortex the basal ganglia and the cerebellum have been reported and a minor degree of inflammatory reaction has been found occasionally Unfortunately most of these pathological changes may have been due to terminal phenomena and not to the chorea itself

Chorea is almost exclusively a disease of childhood The onset before the age of 5 is rare A first attack after 15 is also uncommon except occasionally during pregnancy in the early twenties Females are affected twice as frequently as males

Clinical Picture The characteristic features are involuntary movements with inco ordination muscular weakness and psychic changes The symptoms may come on gradually or suddenly after some emotional disturbance All external stimuli worsen the symptoms An emotional upset probably calls attention to mild symptoms that had previously escaped notice The severity of the symptoms fluctuates greatly When mild there may be nothing beyond general restlessness some grimacing and a minor degree of inco ordination in movements when very severe involuntary movements may be so disturbed as to produce complete incapacity

The involuntary movements are jerky and purposeless usually not immediately repetitive and may be superimposed upon and disorganize voluntary movements Thus flinging movements of the legs may make walking difficult or impossible and involuntary movements of the face tongue and palate may produce dysarthria which may be so distressing that the child becomes mute rather than talks Movements of the abdominal wall and trunk may alter the respiratory rate *Usually the involuntary movements are most severe in the upper limbs* In about a third of the cases there is a great asymmetry between the two sides and rarely the movements are confined entirely to one side The involuntary movements disappear entirely when the patient is asleep except in the very acute cases Voluntary contraction of muscle is weak and sustained effort is difficult or impossible Inco ordination is present and objects may be dropped or thrown Very rarely the weakness and hypotonia are so great that the limb appears to be paralysed Muscles do not atrophy and contractures or fixation in abnormal postures do not occur The outstretched hands are held in a characteristic position with the wrist sharply flexed and the proximal and terminal phalanges of the fingers hyperextended Pronation of the forearm and hands when the arms are put above the head is commonly present The cranial nerves are unaffected apart from the involuntary movements There are no sensory changes *The tendon reflexes may be increased or temporarily absent* The knee jerks may be pendular that is the leg continues to swing after the reflex has been elicited Occasionally however the quadriceps contracts sharply during the phase of knee extension which is therefore prolonged producing the so-called *hung up reflex* *The plantar responses are usually flexor* There are minor mental changes including fretfulness irritability instability or sometimes apathy and sleep may be interfered with by night mares or unpleasant dreams In severe cases confusion agitation hallucinations and delusions may occur During pregnancy the disease is usually much more severe and mental symptoms are common

The temperature and pulse are normal unless carditis or rheumatism are present The cerebrospinal fluid is normal in most cases though occasionally a few cells are found The E E G is either normal or shows non specific changes.

Course and Complications The usual complications are the manifestations of rheumatic infection elsewhere Cardiac complication are said to occur in about 20 per cent of the cases

Acute chorea is relatively benign and complete recovery is the rule unless complications are present The mortality rate of 2 per cent is chiefly due to the cardiac complications though in the severe cases particularly in chorea gravidarum which develops during pregnancy death may result from exhaustion produced by the violent movements The duration of the symptoms varies from 3 weeks to 3 months though minor involuntary movements may persist for many years Recurrences occur in about a third of the patients

Treatment No treatment has any proven effect *on the course of the disease Bed rest is needed* in the severe cases The movements can be lessened by the reduction of all external stimuli and by sedatives such as phenobarbitone 30–60 mg (½ to 1 gr) or chloral 0 3 g to 0 6 g (5–10 gr) thrice daily In the worst cases more powerful drugs such as paraldehyde may be required

Huntington s Chorea

Huntingdon s chorea or chronic progressive chorea is a *hereditary disease of the basal ganglia and cerebral cortex* The pathological changes are widespread degeneration in the entire brain with great shrinking of the caudate and lenticular nuclei and atrophy of the convolutions Where the atrophy occurs there is great reduction in the number of nerve cells and the remaining nerve cells show degeneration

The disease is relatively uncommon but in communities in which one or two families are affected the *incidence may be high It is inherited* as a

rapidly advancing there may be cavitation in the putamen and globus pallidus and even in the cortex In the slower cases the lenticular nucleus is shrunken but there may be no cavitation The neurones are decreased in number completely lost or degenerate There is a diffuse increase of the glia with large protoplasmic astrocytes scattered throughout the nervous system There is usually a nodular cirrhosis of the liver which is small and shrunken The spleen is usually enlarged and congested In the cornea are fine golden yellow granules which give rise to one of the diagnostic features of the disorder Recently metabolic studies have shown that there is increased excretion of amino acids in the urine both of patients and of asymptomatic siblings Abnormal concentration of copper has been found in the liver and brain and an increased excretion in the urine There is a decrease of the copper in the blood and of the caeruloplasmin content of the serum The copper oxidase activity of the serum is also greatly decreased These last two findings are probably the metabolic errors which are inherited

Clinical Picture Tremor of the limbs is usually the first symptom occurring even when the limb is at rest but increased by voluntary movements These may be athetoid and writhing or flapping Rigidity soon occurs and resembles in its distribution the rigidity of Parkinsonism the limbs becoming fixed usually in a position of flexion Contractures may develop Voluntary movements are impaired and articulation and swallowing are early affected Speech may become unintelligible and the facies is vacant and expressionless with silly grins or vacuous smiles Loss of emotional control is present and involuntary laughing and crying may occur There is usually some mental deterioration The nervous system is otherwise normal Corneal pigmentation consists of a zone of golden brown granular pigmentation about 2 mm in diameter on the posterior surface of the cornea towards the limbus It is due to a deposit of copper and is diagnostic It has been named after Kayser and Fleischer Symptoms of cirrhosis of the liver may also be present

The course is invariably fatal but varies in its rapidity Fifty per cent of patients are said to die within 6 years

Treatment The best remedy is Dimercaprol (British Anti Lewisite B A L) This is said to result in improvement in the neurological symptoms a decrease in the corneal pigmentation and an increase in the amount of copper excreted in the urine 2 5 mg/kg of body weight is usually given intramuscularly twice daily in 10-day courses every second month

Spasmodic Torticollis

This condition sometimes called wry neck is characterized by a rotated attitude of the head due to clonic or tonic contractions of the cervical muscles It occurs both as the result of organic disease and of hysteria When organic it is often regarded as a limited form of torsion spasm but it may occur as a sequel to encephalitis lethargica with or without Parkinsonism or as part of other extrapyramidal syndromes

Clinical Picture The development is usually insidious but occasionally—particularly when hysterical—it may be quite sudden The rotation of the head is produced by contraction of the superficial and deep cervical muscles The resulting posture varies according to the muscles affected The disturbance may be mainly tonic giving sustained postures or consist of repeated clonic jerks particularly in hysterical cases There may or may not be resistance to passive movement of the head in the direction opposite to the abnormal position Occasionally the rotation is associated with spasm of the facial muscles and platysma on the side to which the head is rotated or even torsion movements of the upper limb Often the patient can inhibit the torticollis by exerting slight pressure with his finger upon the jaw on the side to which the head is rotated The movement always ceases during sleep Pain may occur in the cervical muscles There are no abnormal findings in the nervous system unless a cervical spondylosis is produced by the continuous movements

The distinction between hysterical and organic torticollis is extremely difficult Hysteria should be suspected when the disorder develops in circumstances of stress though this may be a precipitating factor in the organic variety

The outlook is bad and in most cases little or no improvement occurs Occasionally however when it is due to hysteria psychotherapy may produce improvement and even relief In the organic cases cutting the muscles which are in spasm or their nerve supply has been tried but in a number the spasm later recurs

Athetosis

Athetosis is a condition in which involuntary movements occur on one or both sides of the body The movements are absolutely typical There are facial grimaces often with involuntary laughing and crying writhing movements of the tongue and protrusion of the lips which affects articulation and even swallowing In the upper limbs the movements are most marked at the periphery and the hand has a characteristic posture produced by flexion of the

dysarthric with a monotonous slightly high pitched voice often with a very poor volume so that the patient can hardly be heard Eating a meal takes a long time because chewing is so slow The voluntary part of swallowing is also slow though the auto matic act of deglutition is normal In addition saliva tends to collect and run from the mouth The limb muscles are not atrophied but power is occasionally impaired probably because of the ex cessive rigidity While posture and gait may be normal at first there is soon stiffness of a leg and of an arm with lack of swinging while walking

In advanced cases the posture is one of flexion with the head forward the shoulders stooped and the back bowed forward Both arms are held flexed at the elbow and abducted at the shoulder The gait is slow and shuffling and the patient may have diffi culty in starting to walk often standing for a few seconds before he can get away Occasionally after an initial difficulty in starting there is a rapid in crease in the steps until they break into a short run (the festinant gait) When this occurs there may be difficulty in stopping Occasionally the patient tends to walk backwards All movements are slowly performed and associated movements are usually absent The time needed for dressing eating and other motor activities is greatly increased Writing usually tends to get smaller as the disease goes on The muscular rigidity may become so severe as to paralyse the patient The increase of tone is of a characteristic type and is demonstrated by the inter ruption of passive movements by a series of jerks (cogwheel rigidity) The tremor is coarse usually at the rate of 3–6/sec and regularly alternates between agonist and antagonist It may be confined to any one part of the body is most prominent when the limb is at rest and ceases temporarily when voluntary movements of the affected limb are made It disappears during sleep

Sensation is unaffected The reflexes are normal except when there is excessive rigidity when they are depressed The plantar responses are normal Hyperidrosis undue sensitivity to heat and some times excessive salivation are present

Intellectual functions are unimpaired though the patient may be difficult to understand Mood dis turbances are not uncommon Occasionally there is said to be a rigidity of thought and outlook compar able with rigidity of the muscles

The blood urine and cerebro spinal fluid are normal

As a rule the differential diagnosis between idio pathic and symptomatic Parkinsonism can only be made on the history Post encephalitic Parkinsonism is indicated when the symptoms develop after an acute febrile illness though encephalitis lethargica is almost non-existent at present Tics spasms torticollis oculogyric crises or respiratory disorders are characteristic of the post encephalitic form. In this an obsessional neurosis or occasionally a failure of social morality with delinquency or psychopathy may also develop

Course Whatever its cause Parkinsonism is pro gressive The course may be fairly rapid but in the majority of cases it lasts 15 or more years Death is usually the result of some intercurrent disorder or inanition because of the difficulty in feeding

Treatment Treatment is entirely symptomatic and the results are very variable Both the solana ceous drugs and synthetic compounds with similar pharmacological actions but with fewer side effects are used The solanaceous group includes atropine stramonium and belladonna and hyoscine usually in the maximum dose that the patient will tolerate after it has been gradually increased The synthetic group includes benzhexol (Artane Pipanol) procy clidine hydrochloride (Kemadrin) ethopropazine hydrochloride (Lysivane) and Disipal These too should be given in small doses at first and increased to the maximum the patient will tolerate In the elderly particularly the arteriosclerotic all the drugs of both groups may produce confusional states

It cannot be laid down which of these drugs is likely to give the best results there being many idio syncrasies If one fails to give much improvement others should be tried in turn until the most effec tive is found which is then continued indefinitely Occasional patients will not tolerate an effective dose of any one drug they can sometimes be helped by using a combination of drugs in small doses which cause less toxic effects Supplementing these drugs with anti histamines sometimes increases their potency The amphetamine group may also be added to give the patient more energy to combat his rigidity

Surgical treatment has been tried including re moval of areas in the frontal cortex damage to the basal ganglia by stereotaxis or section of the pyra midal tract in the cervical spinal cord So far these operative procedures are still on trial but stereotoxic destruction of the globus pallidus appears the most promising

Hepaticolenticular Degeneration (Wilson's Disease)

This is a familial disease of great importance in showing the effect of an inborn error of metabolism on the nervous system It begins between the ages of 10 and 25

The pathological changes are widespread involv ing mainly the basal ganglia and to a lesser degree cortex cerebellum and brain stem In the basal ganglia the changes vary in severity and when

minor involuntary movements but usually there is a physical handicap requiring special care and education throughout childhood

Treatment is by intensive physiotherapy and special education Correction of the deformities by orthopaedic surgery may help considerably By devoted care results can be obtained which are often much better than can be expected when the patient is first seen

Congenital and Infantile Hemiplegia

Congenital hemiplegia is very rare Most commonly the infantile hemiplegias occur as a complication of many acute infective disorders of childhood particularly whooping cough The relationship of the hemiplegia to the infection is obscure and frequently the cerebral lesion itself results from a vascular thrombosis

The pathological changes are very varied Brains which are examined later in life may show porencephaly localized cysts or a generalized atrophy of the hemisphere

Clinical Picture Infantile hemiplegia usually develops suddenly though it may pass unnoticed during the primary illness Frequently the first manifestation is a series of fits followed by coma When the patient recovers consciousness he is found to have a flaccid hemiplegia and if the dominant hemisphere is affected he is usually aphasic and perhaps even mentally defective The hemiplegia may recover as the patient recovers from the primary illness but if it does not the flaccidity is followed by spasticity usually in an attitude of flexion The development of the paralysed limbs is retarded and they remain smaller than those of the normal side and contractures develop Epilepsy occurs in approximately half the patients The convulsions are usually focal but rapidly become generalized with loss of consciousness Frequently there is an associated behaviour disorder shown by difficulty in self control or temper tantrums Occasionally athetoid or choreic movements develop

The outlook varies with the severity of the disorder In mild cases education may enable the limbs to be used particularly if great care in after treatment is taken Hope of improvement should not be given up until at least a year or two has elapsed after the onset of the illness

Treatment. In the acute stages the primary condition must be treated Lumbar puncture up to 2 or 3 times daily to reduced the cerebro spinal fluid pressure to normal often diminishes the number of seizures These should also be controlled by paraldehyde Nasal feeding will be required so long as the patient is comatose After recovery of consciousness the hemiplegia is treated by local measures to relax the spastic muscles followed by re-educative exercises Orthopaedic correction of deformities may be needed later Small doses of phenobarbitone should be given for some years in the hope of preventing epilepsy If epilepsy does develop anti-convulsants should be increased to the maximum that the patient will tolerate though the results may be disappointing Recently surgery has been tried the affected hemisphere apart from the basal ganglia being removed almost completely This frequently lessens the fits and improves behaviour disturbances without increasing the disability (except for the addition of a hemianopia)

The Hereditary Ataxias

These are not very common familial or hereditary disorders in which there is degeneration in the cerebellum brain stem and spinal cord The cases vary considerably though any one family usually has a common type of disorder

Spino-cerebellar Ataxia (Friedreich s Ataxia) The symptoms usually develop between the 6th and 13th years though occasionally they appear in infancy and rarely their onset is delayed until 30 Abortive forms in which there are only one or two features of the disease are frequent in some members of a family Ataxia on walking is the most common symptom and usually the first to be obvious It may appear between the 5th and 10th years in a child who has apparently been normal previously though careful cross-examination of the parents may elicit a history of minor clumsiness of the legs even earlier than this A few years after the onset of walking difficulty the upper limb movements becomes ataxic and finally the trunk is involved The movements are jerky awkward and poorly controlled and intention tremor particularly of the extremities is present Titubation of the head or trunk may occur There is a marked ataxic dysarthria with slurring of the speech which may finally become unintelligible Pseudo athetoid and choreiform movements of the extremities may be seen Weakness is common and occasionally there is an almost complete paralysis of the legs with a paraplegia in flexion flabby muscles and disuse atrophy Localized atrophy of the muscles most marked in the forearms and legs but also in the girdle and trunk sometimes may occur in the late stages

Loss of vibration sense in the extremities develops early Impairment of position sense may affect the toes later the fingers and occasionally the trunk to such an extent that the patient has to be supported even when sitting in a chair Superficial sensory loss of a minor kind and some impairment of

wrist and metacarpophalangeal joints and extension of the interphalangeal joints with the thumb adducted and extended Superimposed upon this are *slow writhing movements* of flexion and extension of the wrist and fingers Movements may also occur at the shoulder and elbow and if they are unilateral and sufficiently severe the patient always tries to restrain the affected limb by grasping it with the other The movements are almost always severe enough to interfere with voluntary movement In the lower limb the foot is most affected and is maintained in a position of talipes equinovarus with marked dorsiflexion of the great toe Athetosis is exaggerated by an attempt to use the limbs and by nervousness and excitement It diminishes during relaxation and disappears during sleep Muscular contractures may develop

The cause of bilateral athetosis is usually a congenital abnormality of the corpus striatum though occasionally it results from degeneration of the corpus striatum Unilateral athetosis may also be congenital and is then usually associated with infantile hemiplegia but it may also result from a focal lesion involving the corpus striatum at any age

Treatment is disappointing Sedatives may be tried and re education and relaxation exercises sometimes produce a little benefit Excising the precentral convolution corresponding to the affected limb and dividing the extrapyramidal tracts in the anterior column of the spinal cord above the cervical enlargement have both been tried Unfortunately the movements often return with the postoperative recovery of power in the limb

Congenital and Degenerative Disorders

Congenital Spastic Paralysis, or Diplegia

This term is used to cover a group of cases probably of mixed causation characterized by bilateral and symmetrical disturbance of motility present from birth which may remain stationary or even improve The lesion involves the pyramidal tracts and weakness and spasticity mainly in the lower limbs are the most conspicuous features Other parts of the nervous system may also be involved producing mental defect involuntary movements and ataxia Between 1 and 2 per 1 000 of the school population and 0 5 per 1 000 of the adult population in Britain are thought to be spastics

There are many views as to the aetiology Injury to the brain at birth through meningeal haemorrhage asphyxia at birth prematurity causing an arrest of myelination of the nervous system maldevelopment of the brain and some toxic action early in foetal life producing an arrest in development or even degeneration of parts of the nervous system have all been incriminated The latter is the most probable theory in the majority of patients as it is now known that toxic action during pregnancy can produce developmental defects For instance the occurrence of German measles in the pregnant mother fairly early in the pregnancy may result in deafness in the foetus Similarly the administration of cortisone during pregnancy at the appropriate time is said to produce cleft palate and hare lip Experimentally too it has been shown that X ray irradiation of the foetus in the rat produces disturbances of development and maldevelopment of the nervous system Clearly therefore the embryonic nervous system is vulnerable and may be subject to damage by toxins nutritional defects and other causes at the critical periods in the development As there are many possible aetiological factors the pathological changes are varied

Clinical Picture This varies greatly According to whether the major damage is to the motor cortex the basal ganglia or the cerebellum cases may be divided into the athetoid or ataxic groups There is however no clear cut dividing line between these groups mixed cases being the rule rather than the exception There may also be signs of damage to other parts of the nervous system Approximately half the patients are mentally retarded and in addition defects of speech and motor function may seriously interfere with the intellectual performance

Severe damage to the brain may be obvious at birth by difficulty in feeding poverty of movements and listlessness Frequently it only becomes apparent between 6 months and 2 years from the failure of the infant to hold its head up sit up crawl walk or talk at the expected times and from the appearance of abnormal movements In milder cases the defect may not become apparent for several years when signs of physical inadequacy develop

The course of the disorder is very variable The symptoms usually reach their maximum severity between the ages of 2 and 3 after which there may be some improvement as the patient learns to compensate and benefits from training The disorder may be so mild that the patient reaches adult life with only minor spasticity of the extremities or

spastic paraplegia Cramps and painful spasms in the muscles may then be present

The symptoms of the lower motor neurone degeneration are weakness wasting and fasciculation The latter may be limited to the muscles undergoing active degeneration or may be very widespread The disease is not frequently symmetrical and it tends to spread up a limb in a segmental distribution When lower motor neurone degeneration affects the face lips tongue and palate there is difficulty in pursing the lips whistling is impossible and saliva may run from the open mouth Protrusion of the tongue is weak and then lost and speech suffers severely The patient may become completely mute but phonation suffers very little Swallowing may become increasingly difficult and food may regurgitate through the nose Semi solids are usually easier to swallow than either solids or fluids In the lower limbs the dorsiflexors of the foot are the first to be affected In the final stages weakness of the trunk muscles makes it impossible for the patient to sit up and the respiratory muscles may become weak producing an increasing dyspnoea

The electrical reactions are usually well preserved but electromyography shows spontaneous fasciculation particularly on needle insertion Evidence of degeneration of the lower motor neurone may be found by the presence of fibrillation action potentials and there is usually a marked reduction of the number of spikes on maximal contraction

Upper motor neurone degeneration may be present at any stage of the disease or may predominate and frequently affects the lower limbs (where the lower motor neurone disorder begins late) This causes weakness which is much greater than the severity and extent of the wasting would suggest and the deep reflexes are increased in spite of the wasting The bulbar supplied muscles become very weak from the superimposition of the pyramidal weakness on the lower motor weakness—that is a pseudo bulbar palsy combined with a bulbar palsy —with resultant dysarthria and dysphagia The jaw jerk and palatal and pharyngeal reflexes are exaggerated The pseudo bulbar palsy when severe may lead to an impairment of voluntary control over emotional reactions with paroxysmal attacks of involuntary laughing and crying Sometimes the emotional response may be quite inappropriate producing paradoxical laughing and crying

The sphincters are not affected except in the final stages but occasionally impotence develops Sensory changes are uncommon apart from muscular pain in the early stages Rarely some impairment of cutaneous and deep sensibility occurs Mental changes are absent, though the impairment of emotional control may suggest their presence

Motor neurone disease is steadily progressive though its rate may fluctuate considerably In a small number of cases particularly those with early bulbar affection the patient rapidly deteriorates whereas those with only lower motor neurone affection may go on for a long time The duration of life varies from a year in the most rapid cases to 10 or 12 years in the most chronic

No treatment has any proven effect on the course of the disease and the patient should be encouraged to keep going as long as he can It is perhaps justifiable to give massage and other remedies in the hope of maintaining the patient s morale If nothing is done he will be apt to get into the hands of quacks who may soon leave him without money as well as without hope

Peroneal Muscular Atrophy

This is a relatively rare hereditary form of muscular atrophy The main pathological changes are an interstitial neuritis of branches of the peripheral nerves There are also changes in the spinal cord particularly in the anterior horn cells and in the cells of Clark s column with some degeneration of the dorsal columns and later even of the pyramidal tracts The affected muscles show simple atrophy

Clinical Picture The first symptoms are muscular wasting and weakness usually in the dorsiflexors of the toes and feet. Club foot with a laborious clumsy gait, occurs almost invariably The atrophy spreads up the leg particularly its posterior surface giving a very thin limb but it always stops below the half way point of the thigh The hands do not usually begin to waste until a number of years after the feet though rarely they are affected simultaneously Again the atrophy spreads slowly up the limbs rarely extending above the elbows The tendon reflexes vary most frequently they are diminished or lost in the wasted muscles The plantar responses are usually lost Sensation is always affected though only keen examination may detect this Vibration sense is diminished over the feet and cutaneous sensibility may be disturbed over the periphery of the limbs Deep sensibility is less often affected. The sphincters are always normal The cranial nerves are never affected The electrical reactions show a diminution or absence of the response to Faradism Other members of the family may show only fragments of the disorder the common findings being a claw foot and absence of the deep reflexes in the lower limbs

The disease runs a very slow course and arrest may occur at any time It does not shorten life and with orthopaedic help the disability may be remarkably little No treatment has any effect

two point discrimination may be present The knee and ankle jerks are almost always absent and the upper limb reflexes may disappear later The plantar responses are usually extensor but the abdominal and cremasteric responses are preserved Nystagmus of every kind has been described and occasionally optic atrophy is present though palsy of the eye movements is rare The sphincters are usually un impaired except when there is incontinence from mental retardation Convulsions are a little com moner than in the general population Club feet and kyphoscoliosis are usual and there may be a double pes cavus sometimes with talipes varus or equino varus

The blood urine and cerebro spinal fluid are usually normal but there may be abnormalities in the electrocardiogram

Once the disorder has fully developed it usually progresses steadily until the patient is completely incapacitated in the middle twenties Death is due to intercurrent infection Members of the families who have only one or two features usually the skeletal ones of the disorder may however live a perfectly normal life

No treatment influences the course of the disease

Other Varieties These are even more rare than is Friedreich s ataxia They are associated with wasting of the muscles of the extremities spasticity or gross optic atrophy

Cerebellar Degeneration

When this involves the cerebellum alone it is called primary cerebellar degeneration when it in volves both the cerebellum and some of the brain stem nuclei it is called olivo ponto cerebellar atrophy Both conditions develop in middle life or later

The initial symptom of primary cerebellar degen eration is difficulty in walking and turning the patient having a typical wide based ataxic gait There is intention tremor and ataxia in the lower limbs but less in the upper limbs Dysarthria may develop nystagmus is said to be absent The course is moderately rapid the patient dying in a few years

In olivo ponto cerebellar atrophy there is also a progressive cerebellar ataxia of the trunk and ex tremities with a disorder of equilibrium and gait and slowness of voluntary movements There may be nystagmoid jerks and there is almost always an oscillatory tremor of the head and trunk Extra pyramidal symptoms may occur such as rigidity of muscles and immobile facies and Parkinsonian tremor of the extremities Again the course is slowly progressive incapacity developing in 5–10 years

Cerebellar degeneration can also occur in association with neoplasms elsewhere in the body which have not caused secondary deposits Car cinoma of the ovary may have this effect, and carcinoma of the bronchus may produce a spino cerebellar degeneration Hyperpyrexia may produce a degeneration of the Purkinje s cells of the cere bellum with a cerebellar syndrome

Motor Neurone Disease

(Progressive Muscular Atrophy Amyotrophic Lateral Sclerosis and Progressive Bulbar Palsy)

This disease is characterized by degenerative changes most marked in the anterior horn cells of the spinal cord the motor nuclei of the medulla and the pyramidal tracts and clinically by pro gressive wasting of the muscles

Incidence and Aetiology Three to four per cent of patients admitted to a neurological hospital have this disease Males are affected two or three times as frequently as females It may occur at any age but is chiefly found in middle life Apart from the natives on the island of Guam inheritance does not seem to play any significant part

It has been suggested that the disease may be due to an inborn predisposition to degeneration of the motor neurones (abiotrophy) but this concept is vague and has been generally abandoned It has also been suggested that the disease is due to a toxin with a predilection for the anterior horn cells It is how ever more probably due to disturbance of the en zyme systems in the motor cells and may well be metabolic in origin Very rarely motor neurone dis ease develops in an individual who has previously had an attack of acute anterior poliomyelitis This may be coincidental but as the motor neurone dis ease is mainly limited to the region affected by the poliomyelitis the previous inflammation may have rendered them liable to degenerate later if exposed to other toxins or to metabolic disorders There is no evidence that trauma plays any part though the weakness and wasting may first appear in the muscles most used by the patient in his occupation

Clinical Picture The disease is usually chronic but may be subacute and the onset is therefore generally insidious The earliest symptoms depend on the part of the nervous system first affected Most commonly the patient becomes aware of weakness stiffness or clumsiness of movements of the fingers or of fasciculation and twitching of the muscles If the shoulder girdle is affected the first symptom is weakness of abduction of the shoulder If the degeneration begins in the bulbar motor nuclei the first symptom may be dysarthria or fasciculation of the lips and tongue Less fre quently the lower limbs are affected by wasting and weakness Occasionally the disease begins as a

possible In most cases the symptoms begin in childhood or in young adult life There are many varieties of the disease The pseudo hypertrophic form beginning in childhood is most characteristic The juvenile form occurs usually during adolescence and has no pseudo hypertrophy In the facio scapulo humeral type there is extensive involvement of the facial muscles and the shoulder girdle

Clinical Picture The symptoms are those of muscular weakness In the majority of patients the pelvic girdles are more severely affected than any others Walking is therefore clumsy with a characteristic waddling gait and there is difficulty in climbing up and down stairs or in riding a bicycle Weakness of the shoulder girdle muscles makes it difficult to raise the arms over the head or lift heavy objects

If the facial muscles are affected there is a mask like face with difficulty in closing the eyes and diminution of facial movements The palate or pharyngeal muscles are rarely affected Pseudo hypertrophy affects mainly the gastrocnemius the deltoid the triceps and the spinati There is an advanced degree of lumbar lordosis due to the weakness of the trunk muscles Movements of the arm are accompanied by winging of the scapula There is a characteristic and diagnostic manner of getting up from the horizontal position The patient turns over on to the abdomen and raises the trunk to the crawling position The feet are then placed firmly on the floor with the aid of the arms and gradually the upper part of the body is elevated by climbing up the legs and the trunk Hypertrophic muscles feel firm and rubbery atrophic muscles feel flabby The musculature is usually symmetrically involved and there are no abnormal movements or fasciculation Sensation is normal there are no sphincter disturbances and pain is rare The reflects are lost as the muscles atrophy The cutaneous reflexes are unaffected There are no cerebral symptoms apart from occasional mental retardation

Investigations Blood urine and cerebro spinal fluid are normal The excretion of creatinine is decreased and of creatin increased Ingested creatin cannot be stored Biopsy of muscle shows diagnostic changes Electromyography shows characteristic myopathic break up or fragmentation of the motor unit potentials Frequently there are electrocardiographic changes

Prognosis and Treatment The course of the disorder varies *from a few to many years The earlier* the onset the more rapid the downhill progress Death is due to intercurrent infection or to involvement of the bulbar respiratory or cardiac musculature

No treatment is effective in arresting the disease The good results reported from the use of glycine wheat germ oil vitamin E and alpha tocopherol have not been confirmed Nursing care is all that can be offered

Myotonia Atrophica (Dystrophia Myotonica)

This is an hereditary degenerative disease characterized by myotonia and atrophy of muscles especially of the face and neck cataracts early baldness testicular atrophy and other endocrine dysfunction The aetiology is unknown The changes in the muscles are similar to those which occur in myopathy and consist of hypertrophy and fragmentation of the muscle fibres followed by atrophy Any or all of the endocrine glands may be atrophied with consequent bodily changes The nervous system is never involved

The disease may be transmitted as a dominant or a recessive trait though sporadic cases rarely occur It is more common in the male The onset is usually in the second or third decade Myotonia usually precedes atrophy by several years Siblings may have only the associated disorders such as cataract or early baldness

Clinical Picture The symptoms are dependent upon the failure of the muscles to relax promptly after a forceful contraction This is most likely to occur in cold weather and is exaggerated by emotion The distribution of the myotonia is variable and very rarely all the muscles of the body are affected The presence of myotonia is shown by a slow worm like relaxation of grip when the patient forcefully grasps an object It can sometimes be brought out by percussion of a muscle group which then goes into prolonged contraction followed by slow relaxation The myotonia disappears with the onset of atrophy Any muscles may be affected by atrophy

The sternomastoids and intrinsic muscles of the neck are usually the first muscles to be affected so that the head cannot be lifted and articulation and phonation may be impaired Swallowing is usually spared but the voice is frequently weak and nasal When the facial muscles atrophy the characteristic hatchet face appearance and expressionless facies results Fasciculation does not occur and there is never any hypertrophy Sensation is unaffected and the deep reflexes are normal

In association with this condition cataracts are frequent though they may be found only by slit *lamp examination Mental retardation is not un*common Gonadal atrophy producing early impotence or early menopause early baldness and

Syringomyelia

This is a rare chronic disease characterized by *long funicular cavities in the spinal cord surrounded* by gliosis frequently in relation to the central canal and often extending up into the medulla (syringo bulbia) The commonly accepted theory of causa tion is that *it is the result of abnormal closure of the central canal in the embryo The incomplete* closure leaves cavities around which a secondary gliosis develops The condition is usually sporadic though some familial or hereditary incidence is said to have been established in a few cases It usually begins between the ages of 25 and 35 and affects males three times more frequently than females

A hydromyelia due to dilatation of a normal central canal occasionally develops in association with abnormalities at the base of the skull The clinical picture is similar to that of syringomyelia

Clinical Picture The symptoms develop extremely insidiously Wasting and weakness of the small muscles of the hand or sensory disturbances particularly painless burns on the fingers or fore arm may be noticed first Brachial neuralgia of a peculiarly gnawing character may be early and con tinue even after pain and temperature sense are lost Later there may be weakness and atrophy of the shoulder girdle muscles and a Horner s *syndrome (with ptosis and myosis) due to in* volvement of the cervical sympathetic outflow from the spinal cord Nystagmus is frequent and *vasomotor and trophic disturbances occur in the* upper limbs There is loss of pain and temperature sense usually involving the cervical and upper thoracic dermatomes and absence of the deep reflexes in the upper limbs Spasticity and ataxia of the lower limbs may be added as the cavities en large Sensory involvement below the level of the cavity and sphincter disturbance may also be pre sent Lumbar *syringomyelia is very rare and pro* duces similar manifestations in the lower limbs Syringobulbia is due to the cavity spreading into the lateral cleft of the medulla it produces atrophy and fasciculation of the tongue loss of pain and tem perature sense in one or both sides of the face *nystagmus* dysphonia and dysphagia

The disorder may be strictly unilateral at first the cavitation beginning at the base of the posterior horn and involving the fibres which should eventu ally cross in the anterior commissure of the spinal *cord As the condition progresses it almost always* becomes bilateral and subsequently symmetrical Recent burns the scars of old burns thickening and callus formation in the skin (with coarseness of its texture and localized areas of atrophy or pigmenta tion) and painless sores may all be present The hand may become peculiarly swollen and red—the so-called flesby hand Occasionally terminal phal anges or entire digits are painlessly lost *The joints* of the upper limb are not uncommonly affected becoming Charcot joints usually of the atrophic variety (p 520) Kyphosis scoliosis and club feet are often seen

Investigations apart from occasional evidence of spinal block on lumbar puncture are usually normal

The course of the disorder is slowly *progressive* over many years There may eventually be com *plete incapacity due to the paralysis though* useful work may be prevented by the sensory defects even when the muscular atrophies are relatively slight *Death may be the result of intercurrent* infection or destruction of the medullary nuclei

Treatment Most patients are treated by deep X rays to the affected segments of *the spinal cord or* medulla but whether this does good is uncertain If spinal compression occurs operation to relieve the pressure on the cord by opening the cavity can be attempted Symptomatic treatment should be *given for the ulcers and* other trophic changes

Disorders of Muscle

Muscular Dystrophy

This is a not uncommon *disease of unknown* cause producing atrophy weakness and sometimes pseudo hypertrophy of muscle There are often associated endocrine *disturbances usually of a* multi glandular type but their relationship to the *muscle disorder* is unknown Again a disorder of creatine metabolism is found but whether this is more than expression of the muscular wasting is uncertain

The pathological changes are entirely confined to the muscles The fibres may be enlarged gradu ally split and undergo vacuolization and hyaline de generation with an increase in the number of *sarcolemmal nuclei and* replacement by fat and fibrous tissue

The disease is often heredo familial though sporadic cases occur It may *affect and be trans* mitted by either sex though its incidence is greater in males and various modes of inheritance are

possible In most cases the symptoms begin in childhood or in young adult life There are many varieties of the disease The pseudo hypertrophic form beginning in childhood is most characteristic The juvenile form occurs usually during adolescence and has no pseudo hypertrophy In the facio-scapulo humeral type there is extensive involvement of the facial muscles and the shoulder girdle

Clinical Picture The symptoms are those of muscular weakness In the majority of patients the pelvic girdles are more severely affected than any others Walking is therefore clumsy with a characteristic waddling gait and there is difficulty in climbing up and down stairs or in riding a bicycle Weakness of the shoulder girdle muscles makes it difficult to raise the arms over the head or lift heavy objects

If the facial muscles are affected there is a mask like face with difficulty in closing the eyes and diminution of facial movements The palate or pharyngeal muscles are rarely affected Pseudo hypertrophy affects mainly the gastrocnemius the deltoid the triceps and the spinati There is an advanced degree of lumbar lordosis due to the weakness of the trunk muscles Movements of the arm are accompanied by winging of the scapula There is a characteristic and diagnostic manner of getting up from the horizontal position The patient turns over on to the abdomen and raises the trunk to the crawling position The feet are then placed firmly on the floor with the aid of the arms and gradually the upper part of the body is elevated by climbing up the legs and the trunk Hypertrophic muscles feel firm and rubbery atrophic muscles feel flabby The musculature is usually symmetrically involved and there are no abnormal movements or fasciculation Sensation is normal there are no sphincter disturbances and pain is rare The reflects are lost as the muscles atrophy The cutaneous reflexes are unaffected There are no cerebral symptoms apart from occasional mental retardation

Investigations Blood urine and cerebro spinal fluid are normal The excretion of creatinine is decreased and of creatin increased Ingested creatin cannot be stored Biopsy of muscle shows diagnostic changes Electromyography shows characteristic myopathic break up or fragmentation of the motor unit potentials Frequently there are electrocardiographic changes

Prognosis and Treatment The course of the disorder varies from a few to many years The earlier the onset the more rapid the downhill progress Death is due to intercurrent infection or to involvement of the bulbar respiratory or cardiac musculature

No treatment is effective in arresting the disease The good results reported from the use of glycine wheat germ oil vitamin E and alpha tocopherol have not been confirmed Nursing care is all that can be offered

Myotonia Atrophica (Dystrophia Myotonica)

This is an hereditary degenerative disease characterized by myotonia and atrophy of muscles especially of the face and neck cataracts early baldness testicular atrophy and other endocrine dysfunction The aetiology is unknown The changes in the muscles are similar to those which occur in myopathy and consist of hypertrophy and fragmentation of the muscle fibres followed by atrophy Any or all of the endocrine glands may be atrophied with consequent bodily changes The nervous system is never involved

The disease may be transmitted as a dominant or a recessive trait though sporadic cases rarely occur It is more common in the male The onset is usually in the second or third decade Myotonia usually precedes atrophy by several years Siblings may have only the associated disorders such as cataract or early baldness

Clinical Picture The symptoms are dependent upon the failure of the muscles to relax promptly after a forceful contraction This is most likely to occur in cold weather and is exaggerated by emotion The distribution of the myotonia is variable and very rarely all the muscles of the body are affected The presence of myotonia is shown by a slow worm like relaxation of grip when the patient forcefully grasps an object It can sometimes be brought out by percussion of a muscle group which then goes into prolonged contraction followed by slow relaxation The myotonia disappears with the onset of atrophy Any muscles may be affected by atrophy

The sternomastoids and intrinsic muscles of the neck are usually the first muscles to be affected, so that the head cannot be lifted and articulation and phonation may be impaired Swallowing is usually spared but the voice is frequently weak and nasal When the facial muscles atrophy the characteristic hatchet face appearance and expressionless facies results Fasciculation does not occur and there is never any hypertrophy Sensation is unaffected and the deep reflexes are normal

In association with this condition cataracts are frequent though they may be found only by slit lamp examination Mental retardation is not uncommon Gonadal atrophy producing early impotence or early menopause early baldness and

mild degrees of hypofunction of the pituitary thyroid adrenals or pancreas are all usually present The disease progresses extremely slowly so that the patient may live for very many years

Investigations The blood urine, and cerebro spinal fluid are normal Electrical responses are re duced in the atrophied muscles but in the myotonic muscles a long contraction is produced which relaxes slowly

Treatment The myotonia can be almost com pletely relieved by quinine 0 3–0 6 g (5–10 gr) of any quinine salt should be given 2 or 3 times a day Apart from substitution therapy for the endocrine dysfunction the other features of the disorder cannot be treated

Myasthenia Gravis

This is a chronic disorder of muscle function which is characterized by weakness and abnormal fatiguability of voluntary muscle It is regarded as probably due to a defect of conduction across the myoneural junction but it is affected also by changes in the thyroid and thymus The defect at the myoneural junction may be related to a disorder of acetylcholine metabolism but no deficit in acetyl choline or excess of the acetylcholine esterase has ever been shown However as will be seen later the response to neostigmine is very suggestive

Pathological changes in this disease are few and are found only in the muscles and thymus The muscles often show characteristic collections of lymphocytes (lymphorrages) in the interstitial tissue but there is no change in the muscle fibres around them Often no lymphorrages can be found in what appears to be a typical case Occasionally in late cases some fibre atrophy may be seen The thymus may show a tumour (thymoma) in a quarter to a third of the cases In the majority of the others there is a hyperplasia of the thymus of lymphoid type with the formation of germinal centres in the me dulla

Clinical Picture There are two chief types of the disease a steadily progressive form associated with a thymoma and a remitting relapsing form with lymphoid follicle hyperplasia In this type remis sions lasting from a few months to many years are common

The disease may begin at any age from birth to the eighth decade but is most common between twenty and forty It is equally frequent in the two sexes but more female patients are under thirty and more males over thirty The onset is most commonly insidious Asymmetrical intermittent and often variable weakness of the extra ocular muscles is usually the first symptom Alternating ptosis or squint may be found and the appearance may vary at different times of the day The intrinsic eye muscles are not affected The bulbar supplied muscles are also commonly affected early with re sultant difficulty in chewing swallowing and speak ing Involvement of limbs and trunk occurs much less frequently especially as an initial manifestation The degree and amount of muscle involvement de pends on the severity of the attack and in a bad case almost all the voluntary musculature may be involved including the muscles of respiration In voluntary muscle is spared

The signs which depend on the amount of muscle involvement are those of muscle weakness The most important feature of the weakness is its rela tion to use After a few contractions the power rapidly diminishes and may recover equally quickly with rest The muscles do not ache and are not tender as in true fatigue and only the muscles con tracting are affected The weakness takes an increas ing length of time to recover as the disease progresses and eventually recovery is incomplete so that there is constant though still variable weak ness As the condition deteriorates the danger of sudden death from respiratory failure increases Some atrophy of muscles may occur but this must not be confused with general thinning produced by the difficulty with feeding Reflex and sensory ex amination is normal

Investigations The blood and C S F are normal Increased fatiguability can be shown by electrical stimulation of the muscle E M G examination shows a decrease in the amplitude of the motor units

Diagnosis This depends on the classical story of varying weakness together with the dramatic re sponse to edrophonium (Tensilon) and neostigmine The former is slowly injected intravenously in 10 mg doses and improvement in power is evident in ninety seconds and the whole reaction is over in five minutes There is little unpleasantness about this test which is very rapidly performed Neostig mine is injected subcutaneously in doses of 1 5 to 2 5 mg preceded by 1 mg of atropine fifteen to twenty minutes earlier to prevent the visceral effect of the neostigmine Improvement begins within fifteen to thirty minutes and lasts for four to six hours

The condition has to be differentiated from all diseases which produce weakness in the bulbar sup plied muscles or those of the periphery

Treatment Neostigmine should be given by mouth in doses of 30 mg repeated up to two hourly if necessary Pyridostigmine bromide (Mestinon) which is reputed to be longer acting may alterna tively be used in tablets of 60 mg either alone or

in combination with neostigmine Parenteral injection of neostigmine may be needed to supplement this Adjuvants to treatment are ephedrine (30 mg three times daily) potassium and atropine which is often necessary to control neostigmine colic in doses of up to 0 6 mg Treatment has to be continuous unless a remission occurs but sometimes a state of neostigmine poisoning sets in and the muscles fail to respond to the drug This may call for complete cessation of all treatment and nursing the patient in a respirator and tube feeding until the muscles respond again Thymectomy appears to help in young people with an acute onset unless the gland contains a thymoma when preliminary irradiation may make the operation less of a risk

Maintenance of life for an established case of myasthenia is however precarious though it can go on for many years

Paroxysmal Disorders

Migraine

Migraine is a paroxysmal disorder in which visual hallucinations scotomas and other disturbances of cerebral function are associated with periodic headache The headache is often unilateral and may be followed by nausea or vomiting

The mechanism of migraine is probably two-fold The prodromal manifestations are thought to be due to arterial spasm of the intracerebral vessels and the headache to dilatation of the arteries of the dura and scalp The frequency of migraine has not been accurately determined but it probably affects between 5 and 8 per cent of the population It may be more common in women than in men and there is a hereditary predisposition to it, different series giving figures between 50 and 85 per cent as the familial incidence It is usually more common and more severe in the patient with a personality of the obsessional type producing inflexibility over-conscientiousness and perfectionism This may be associated with feelings of insecurity and tension

Clinical Picture The prominent feature is periodic headache which may be unilateral or generalized It may be localized anywhere in the scalp and varies from a mild discomfort to a completely prostrating throbbing pain Severe attacks are associated with irritability nausea vomiting and photophobia and sometimes with abdominal dysfunction cyanosis of the face or extremities vertigo tremors pallor excessive sweating and chilliness The duration of attacks varies from a few hours to many days.

Headache is the usual presenting symptom, but sometimes an aura precedes it This aura is frequently visual and may include flashes of light, scotomas and quadrantic or hemianopic field defects The usual sensory aura is of paraesthesias which may be widespread and bilateral or involve one half of the body Dysphasia or weakness of one of the extremities are rare If the prodromal symptoms are on one side the headache is usually on the opposite side If the headache or prodromal manifestations are invariably on one side the syndrome is possibly due to a structural abnormality of the intracranial blood vessels

Between the attacks the patient is usually very well. During the attack he may appear acutely ill though there may be no signs or merely dilatation and increased pulsation of the arteries of the scalp which are frequently tender to touch

In most cases there are no neurological signs Very rarely vascular accidents including thrombosis of retinal or cerebral vessels or small haemorrhages from pial retinal or scalp arteries are precipitated by an attack Occasionally cranial nerve palsies occur in an attack producing the so-called ophthalmoplegic migraine In these cases an aneurysm of the carotid artery is likely but is not invariably present.

Investigations The blood urine and cerebrospinal fluid during or between attacks are all normal There may be only minor abnormalities in the electroencephalogram during an attack.

Course and Prognosis. As the patient grows older the attacks which may have been frequent and severe gradually diminish and may eventually die away altogether This is particularly likely to happen after the menopause in women Sometimes migraine is replaced after some years by a periodic recurrent abnormality of some other part of the body This may consist of attacks of abdominal pain with nausea vomiting and diarrhoea or of attacks of pain in other parts of the body

Treatment. For the acute attack analgesics of any kind which suit the patient and which he can retain should be given Frequently they are useless and the only drug which helps is ergot, either as ergotamine tartrate or dihydroergotamine These are most effective when given parenterally as early in the course of an attack as possible and act by constricting the dilated vessels ½ mg of ergotamine tartrate subcutaneously is the usual dose but it may produce vomiting. By mouth ergotamine products are less useful probably because vomiting or closure of the pylorus prevents absorption though 2 or 3 mg

of ergotamine tartrate usually combined with caffeine and repeated in half an hour if necessary may be effective Vomiting which prevents the absorption of these substances can sometimes be prevented by giving prochlorperazine (Stematil) at the same time Ergot preparations can be given by suppository and though less effective than injections *may be of some value*

Between attacks intermittent courses of tension relaxing drugs such as sodium amytal 60 mg (1 gr) b d can be quite useful *in diminishing the frequency* of the attacks Urea 2 g t d s p c or acetazolamide (Diamox) 125 mg b i d are also said to be helpful Desensitization may be tried if any specific food or substance can be found to which the patient reacts by headache otherwise non specific desensitization with histamine perhaps combined with steroids may be helpful Surgical section of the branches of the external cartotid has been tried if the headache is fairly sharply localized but as a *rule the headache spreads to other regions after* an interval Systematic psychotherapy may be of help in some patients

Epilepsy

This is a paroxysmal transitory disturbance of the brain function developing suddenly and ceasing spontaneously with a great tendency to recur An adequate definition is still lacking but the following attempts to cover both causation and effects in a comprehensive fashion Epilepsy is a recurrent disturbance in the chemico electrical activity of the brain which *manifests* itself in a *symptom complex* of which impairment of consciousness perturbation of the autonomic nervous system convulsive movements sensory abnormalities or psychic disturbances are the essential components (Lennox)

Epilepsy presents a social and economic problem of some size for its incidence is approximately 1 in 200 of the population *at some time or other during* their lives Men and women are equally affected The hereditary element in epilepsy is well recognized and abnormal electroencephalograms are six times as common in the relatives of epileptic patients as in non epileptic patients though these abnormalities are generally non specific The familial abnormality of the E E G *in the relatives* of epileptics is almost as common when the epilepsy is symptomatic as when it is idiopathic thus indicating *that in* all forms of epilepsy some inherited factor is usually present

Aetiology A great number of biochemical and physiological studies have been made on patients with convulsive seizures but the pathophysiology is still unknown Convulsions may be produced by a *great variety of conditions such* as acute anoxaemia of the brain hypocalcaemia hypoglycaemia and over hydration yet these factors are rarely found in epileptic patients Again seizures occur frequently with organic lesions of the brain but gross damage to the brain is not found in very many epileptics In any event a constant cause such as an area of brain damage cannot be the only factor responsible for seizures because the abnormality is present continuously whereas the seizures *occur only at irregular intervals Neither can the* so called epileptogenic scar following damage to the brain be regarded as the focus of an abnormal discharge as the scar *is probably completely* inert The normal or nearly normal tissues adjacent to the injured area are the more likely site of the epileptic discharges

For practical purposes epileptics are often divided into primary or idiopathic and secondary or symptomatic though in most symptomatic epilepsies a *hereditary factor* which varies in importance from patient to patient is also present Indeed there is good evidence that most epilepsies are of *mixed origin a genetic factor* and an acquired factor being present in varying degrees Given a predisposition to seizures almost any abnormality of the brain seems to be a precipitating factor Changes which occur early in life in association with intra uterine or birth injuries asphyxia and excessive sedation seem to be particularly significant because the brain *in early life is poorly protected* and unusually sensitive to injury However infections later in life especially those involving the brain or its coverings trauma tumours and the degenerative changes of old people in the blood vessels neurones or glial tissue may also provoke seizures

Idiopathic epilepsy is commoner in *the earlier* years and symptomatic epilepsy increases with increasing age but any variety of epilepsy may occur *at any age Often some arbitrary* age such as 20 or 25 is chosen and any fit occurring for the first time after this age is fully investigated This may be reasonable when enforced by the limitation of clinical and physical methods of investigation but ideally every case calls for a full consideration as without it a planned line of treatment is impossible

Varieties of Epilepsy There are many types of epileptic attack but analyses helped by electro encephalographic studies have demonstrated that there are three large groups into which most fits can be placed

(a) Grand Mal Attacks

This is the *classical fit which* in its full motor form has an aura a tonic phase a clonic phase

and a post epileptic state Fractions of a fit con sisting of only one or more phases may occur This is well seen in the focal or Jacksonian motor attack which may consist only of localized contractions of a few muscle groups A fractionated fit may re main as such or may pass into a full blown fit In any case of grand mal whether partial or complete the muscle contractions take the same form All the muscles moving a joint—agonists antagonists and synergic groups—contract together the resulting often bizarre posture depending on the relative strengths of the different groups This indicates that there has been a simultaneous discharge of cortical neurones and results in a movement which is quite unorganized and bears no relation to the function of the part It corresponds electroencephalographi cally to the discharge of the fast waves from the cortex which like the fit may be localized to one area or may be symmetrical and generalized So long as movements and cortical discharge are limited to one area consciousness is not lost but when movements are bilateral consciousness is nearly always lost Similarly when the tingling or flashes of light of the sensory attacks are uni lateral or localized change of consciousness usually does not occur

The tonic phase of the attack usually lasts 1 or 2 minutes and is associated with increasing cyanosis due to cessation of respiration Depletion of oxygen probably brings the tonic phase to an end and the body may relax quite rapidly the cyanosis dis appearing as a sharp breath is taken However with the improvement on oxygenation the clonic phase may begin which consists of a broken up tonic phase the various convulsive movements being again the result of a completely unorganized dis charge The tongue may be bitten and incontinence of urine often occurs The jerks become progres sively less marked and shorter until they die away completely The patient may remain unconscious for up to half an hour and on recovery of con sciousness is confused and may pass into a post epileptic stupor or sleep Headache is common after the attack and occasionally vomiting occurs Some times instead of sleep an abnormal mental state supervenes lasting minutes to an hour in which automatic actions are carried out although the patient looks completely conscious

As already mentioned the patient may have only a fraction of a grand mal attack consisting perhaps only of the aura or of a very short lived attack fol lowed by a post epileptic state which lasts much longer Sometimes the whole attack may be so brief as to be almost indistinguishable from petit mal but still has the electroencephalographic features of a grand mal attack

(b) Petit Mal Attacks

This is a brief interruption of consciousness with no other change in the thought processes There may be little or no bodily manifestations of change or only be a staring expression of the eyes a move ment of the eyes upwards or blinking at the rate of about 3/sec Movements of the extremities may be momentarily retarded or arrested there may be a short sharp movement of all extremities (myo clonic jerks) or the patient may fall to the ground due to a sudden loss of postural control with com plete muscular hypotonia (akinetic attacks) Some times a petit mal attack precedes a grand mal attack Occasionally the patient continues with whatever he is doing though he can do nothing that requires conscious control There is no confusion after the attacks

Petit mal attacks are thought to originate in the thalamus and produce simultaneous inactivation of the cortex for a short period thus giving rise to the inhibitory features of the attack They are never seen following lesions acquired more than a short period after birth and may be taken as certain evidence of idiopathic epilepsy As many as 80 or 100 attacks may occur in an hour This state is occasionally known as pyknolepsy

(c) Psychomotor Attacks

In these attacks organized movements sensations or emotions occur The muscular contractions are orderly agonists and antagonists following one an other as demanded by reciprocal innervation and the movement may even appear purposive Sensory disturbances may be mainly affective such as fear pleasure or compulsive urges Somatic sensory manifestations may affect the body as a whole giving micropsia or macropsia The déjà vu pheno menon (sudden feelings of intense familiarity) or complete depersonalization with feelings of un familiarity may occur These manifestations may all be linked together These attacks seem to originate in the anterior part of the temporal lobe

Minor attacks of psychomotor epilepsy are similar to petit mal being brief and the patient does not usually fall to the ground in coma Their duration is however a little longer from 30 sec to 2 min and the range of muscular movements is greater There are frequently twisting or writhing movements of the extremities smacking movements of the lips an attempt at incoherent speech and in voluntary performance of what may seem to be purposeful activity As a rule consciousness is a little more clouded than in petit mal and the patient has complete amnesia for the entire attack and sometimes for a short period after it An abnormal

sensation in the abdomen is an occasional feature of this type of epilepsy

Status Epilepticus

The average incidence of grand mal attacks is rarely more than once or twice a day but they tend to occur in groups Thus attacks may occur every day or two until there have been up to 6 or 7 and there is then a relatively long gap as though the epileptic tendency had exhausted itself for the time being Occasionally however attacks follow each other without recovery of consciousness If there are several in succession status epilepticus is said to be present This particularly occurs in chronic epileptics who have suddenly omitted or reduced their treatment Occasionally however it ushers in epilepsy due to organic disease In any event it is an extremely dangerous condition and if not quickly stopped the patient may die of exhaustion and hyper pyrexia

Focal status in which focal attacks succeed one another very frequently occasionally occurs It is not at all dangerous unless grand mal attacks supervene Rarely continuous twitchings in a small group of muscles persist for many hours This is frequently due to a focal discharge and is then known as epilepsia partialis continuans

Reflex Epilepsy

Occasionally an epileptic attack is apparently precipitated by a given stimulus it is then regarded as a reflex epilepsy Being startled by pain or noise is the most frequent stimulus A brief epileptic attack causing merely transient loss of consciousness and resembling a faint may occur after minor injury An unpleasant sight sound or smell or even an unpleasant association such as the typical smell of hospital may also precipitate an attack Rarely there is a very specific stimulus If this is some particular music or reading matter musicogenic reflex epilepsy or dyslexic reflex epilepsy are said to be present

Post-epileptic Automatism

Even brief epileptic attacks are occasionally followed by a period of altered consciousness in which automatic actions are carried out To the onlooker these may appear purposive and may be of great medico legal importance If automatism following a fit is not witnessed it is difficult to be sure from a description that it has actually occurred This is particularly so when post epileptic automatism is advanced as a defence for some abnormal behaviour The criteria which characterize automatic actions are that they are performed without the need for reasoning and however complicated they may seem to the observer, they fit into the normal pattern of the everyday life of the individual Though these criteria may not cover all post epileptic automatism they account for most cases

Aura Auras may be of very many kinds Frequently an aura is so short that it is lost in a post epileptic amnesia so that the patient says he has had no warning whatsoever Sometimes the aura is merely a feeling of discomfort in the abdomen or a sense of uneasiness or of something impending and the patient may from previous experience then be aware that an attack is about to occur Frequently the aura is related to a focal discharge and may then be of great localizing value The uncinate attack is a particularly well known aura in which the patient is aware of a smell or taste which he usually cannot describe except to say it is unpleasant This may then be followed by other features of a temporal lobe attack or by a grand mal attack Auras due to focal attacks arising in the sensory areas are as has already been mentioned usually unorganized consisting merely of curious pins and needles flashes of light or odd noises or sounds However if the higher sensory areas are involved a much more organized form of aura may be present The patient may actually see a formed object such as a coloured round globe or hear words though he may not be able to distinguish their exact meaning The auras are usually stereotyped and even though the patient cannot describe what is heard he will be able to say that it is exactly the same as on previous occasions

The Signs No physical findings are diagnostic of epilepsy Scars may be found on the body due to injury or on the tongue or lips following the lacerations Abnormal neurological findings are found in patients in whom the seizures accompany organic disease of the nervous system but these findings are due to the underlying disease not to the seizures However during an attack ext nsor plantar responses and loss of the pupillary reflexes which are directly due to epilepsy are common There may also be loss of the conjunctival and corneal reflexes Occasionally there are signs due to untoward sid actions of the anti convulsant remedies

Associated Behaviour Disorders Mental deterioration is not uncommon in patients with seizures associated with organic lesions of the brain but the majority of patients who have no organic disease of the brain show no deterioration of intellect even though fits are frequent

Epileptics have been said to be egocentric pedantic and emotionally narrow but observation of a large number who live outside institutions particularly if they lead full and normal lives shows that the range of temperament is as wide as in

other groups of the population Disorder of behaviour may however occur during or after a fit or may replace a fit when it is occasionally called an epileptic equivalent When it occurs during a fit it is a positive phenomenon due to abnormal cerebral discharges The behaviour is then usually aggressive apparently purposive bizarre and illogical and is not related to events preceding the attack or to the environment. After the fit abnormal behaviour is the result of confusion and usually has a negative quality The patient can continue with simple routine activity and may even obey simple commands but there is usually a gross defect of understanding initiative and judgment. There is usually complete amnesia for this post-epileptic state Disturbances which replace the attack are less common and seem to consist of a mainly depressive disorder in which accompanying irritability may lead to aggression A psychomotor seizure may consist of a brief period of bad behaviour during which characteristic electroencephalographic changes occur Here the abnormal behaviour is not the result or the accompaniment of epilepsy nor is it an epileptic equivalent it is epilepsy

Investigations Apart from the electroencephalograph changes there are no abnormal findings unless there is organic disease of the brain when the findings are due to the disease not to the epilepsy

The electroencephalogram may reveal the characteristic epileptic waves both in clinical and subclinical attacks There may also be abnormalities in the interseizure record and a focal disturbance too may be shown However a normal curve does not exclude epilepsy because epileptic electrical activity is not continuous in most epileptics and it will be demonstrated only if present at the time of the recording Epileptic wave forms may also be found in people who have no clinical evidence of epilep y because fits only occur if the brain as a whole is receptive of epileptic electrical activity

Diagnosis. In the majority of patients a careful history particularly from an intelligent eye witness will make certain the diagnosis of epilepsy and the electroencephalogram if typical will be confirmatory Convulsive seizures must be distinguished from hysterical attacks This is easy if the patient is observed by an experienced individual but there are no absolute criteria for the differentiation of an hysterical attack from an epileptic seizure The best guide is probably the state of consciousness of the patient If he can be aroused from a major seizure by a sharp stimulus or if the events which transpire during an attack can be recalled epilepsy is unlikely Hysterical attacks often occur in the presence of an audience are precipitated by emotional situations and are not usually followed by headache muscle soreness or mental cloudiness Nevertheless to differentiate between these two phenomena without personal observation is often impossible The differential diagnosis of the cause of epilepsy is to be found under the headings of the various causative conditions

When the electroencephalogram is doubtful measures may be taken to produce a diagnostic epileptic record Such measures include overbreathing for two or three minutes during the recording and a light flickering at different speeds either of which may cause epileptic wave forms to appear Sleep records taken after quinalbarbitone and activation by means of over hydration or analeptics such as leptazol or bemegride (Megimid) may also help

Course and Prognosis. Once the pattern of epileptic seizures has been established for a number of years complete remission is rare Even if intermission due to therapy lasts for 3 to 5 years the attacks may return when the treatment is withdrawn Convulsions in infants and young children under 5 are approximately ten times as common as epilepsy and it is not usually possible to be certain which children with infantile convulsions are likely to develop epilepsy However if convulsions occur with every febrile illness and are very frequent, and particularly if there are abnormalities of the electroencephalogram of epileptic type in the seizure free period epilepsy is likely

Treatment. 1 *Removal of Cause* Factors which precipitate attacks should if possible be eliminated This implies the removal of all operable tumours of the brain evacuation of abscesses and removal of their capsule and considering the removal of scar tissue Chronic infections and endocrine abnormalities such as those which produce hypocalcaemia or hypoglycaemia should also be treated However the patient whose structural abnormalities are dealt with surgically may still go on having epileptic attacks and it is usually advisable to continue with anti-convulsant therapy for a long time after the apparent cause of the epilepsy has been removed

2. *Mental and Physical Hygiene* This implies education both of the patient and of his relations and others who have any contact with him so that he can live a full and normal life For the patient who is reasonably controlled most activities can be permitted and the family should not be allowed to turn him into a chronic invalid Activities which endanger the lives of others such as driving a car should be prohibited Patients should be placed in institutions only if mentally deteriorated or unduly violent or if they have frequent attacks not controllable by treatment since their presence at home may ruin the lives of other members of the family

3 *Drug Treatment* Many drugs are available for the control of epilepsy and the drug should be suited to the nature of the attack as well as to the individual If satisfactory results are *not obtained* with one drug then others should be tried and a combination of two or more drugs often gives better results than one alone A sudden change in the type of therapy may be accompanied by an increase *in the attacks* or even by status epilepticus so a switch from one drug to another should be gradual Phenobarbitone or phenytoin are the drugs of choice in the treatment of grand mal If satisfactory results are not obtained methoin or primidone can be tried and a combination of these drugs is often extremely useful Psychomotor attacks are said to respond best to the hydantoinates such as sodium phenytoin Troxidone paramethadione and phensuximide are the only drugs that influence petit mal

The initial adult dose of phenobarbitone alone is 30 mg (½ gr) three times a day Up to three or even four times this amount can be given if necessary although it is probably better to combine it with sodium phenytoin than to give such high dosage Drowsiness is common with phenobarbitone particularly at first but it disappears with continued use In high dosage it may give rise to rashes and to minor symptoms of cerebellar deficiency such as slurred speech nystagmus and some tendency to ataxia Sodium phenytoin is given in doses of 100 mg (1½ gr) two or three times a day but it can be increased to two or even three times this level Toxic symptoms include nausea vomiting nervousness ataxia hypertrophy of the gums dermatitis and rarely psychotic manifestations and blood dyscrasias If phenytoin is found to be too toxic even after repeated trials methoin (Mesontoin) may be substituted in similar dosage though it tends to produce drowsiness Primidone (Mysoline) is of value in the control of grand mal and psychomotor seizures and may be given alone or together with sodium phenytoin Initially a very small dose such as 60 to 125 mg daily should be given The amount should then be slowly increased to between 1 and 1 75 g (4 to 7 tablets) daily in adults Troxidone (Tridione) helps approximately half the cases of petit mal The dosage varies from 0 3 to 2 7 g daily beginning with a small dose and gradually increasing until the seizures are controlled or toxic symptoms appear Toxic symptoms include skin rashes undue sensitivity to light and blood dyscrasias affecting either the red cells or white cells Routine blood counts are sometimes done monthly in the hope of detecting these blood dyscrasias However it is probably much more important to warn the patient or his family that if any toxic symptoms such as rashes bleeding unsteadiness sore throat or pyrexia develop the drug should be stopped immediately and medical advice sought, as changes in the blood may take place suddenly and *very shortly after* a blood count has been found normal

Amphetamine sulphate or other amphetamine derivatives are used as adjuvants in the treatment of convulsive seizures They are useful in combating the lethargy produced by some of the anti-convulsants and occasionally they seem to reduce the frequency of petit mal attacks in children

While bromides were formerly the main therapeutic agent in epilepsy they have now been replaced almost entirely by the barbiturates and the hydantoinates but when all other drugs fail they may be tried and occasionally produce effective control There is a risk of bromism developing and the chloride intake must be kept at an adequate level to prevent this Acetazolamide (Diamox) has been used with varying success in the treatment of both petit mal and of grand mal in doses of 125 mg 2 or 3 times a day with occasional breaks in therapy to renew its effectiveness

Status Epilepticus This condition must be treated energetically as there is considerable risk of the patient dying as the result of exhaustion or passing into a non reversible coma Probably paraldehyde is the drug of choice and in an adult 10 ml may be given intramuscularly in one injection Alternatively it may be given extremely slowly by intravenous injection If the attacks continue in spite of this further doses of about 5 ml of paraldehyde may be administered up to a total of 50 ml until the attacks are controlled If this fails the safest course is to stop the attacks with a general anaesthetic given by an anaesthetist who has apparatus available for the maintenance of respiration

Tetany

Tetany is a clinical syndrome characterized by an increased irritability of the neuro muscular apparatus It occurs in any condition in which there is a decrease in the ionized calcium content of the serum In many parts of the world its most common cause is rickets but this is now very rare in Britain It is also associated with hypoparathyroidism (true or pseudo) inadequate intake of calcium persistent fatty diarrhoea (steatorrhoea or coeliac disease) prolonged lactation and alkalosis secondary to hyperventilation persistent vomiting or the ingestion of excessive amounts of alkali It is chiefly a disease of infancy and early childhood though it may also occur in older children or adults

Clinical Picture Carpopedal spasm laryngospasm and convulsions are the characteristic symptoms The carpal spasm is an involuntary contrac

tion of the muscles of the upper limbs in which the fingers are flexed at the proximal joint and extended at the two distal joints The wrist and elbow may also be flexed In pedal spasm there is flexion of the toes at the proximal joint and extension of the two distal joints the plantar surface of the foot is con cave The ankle may be extended and the thighs abducted Only in the most severe spasm are volun *tary movements of the fingers and toes lost* *Some* times the muscles of the face or other muscles are affected by spasms which may last for hours or even days If prolonged the spasms are painful and the pain is increased by passive movement

Laryngospasm is due to contraction of the laryngeal muscles The respirations become laboured and there is prolonged inspiratory stridor In severe attacks unconsciousness or convulsive seizures may occur but most commonly there are a few noisy inspiratory gasps and the child then breathes normally until the next spasm de velops Generalized convulsions accompanied by loss of consciousness are common in infants under a year old They may be very frequent

The elicitation of increased neuro muscular irri tability by tapping a nerve as it runs across a bone is the chief sign A spasmodic contraction of the facial muscles may be produced by tapping the facial nerve (Chvostek s sign) Tapping the peroneal nerve as it crosses the head of the fibula has a similar result Trousseau s sign is the production of carpal spasm by squeezing the upper arm either manually or by a pneumatic cuff Erb s sign shows increased neuro muscular activity by electrical stimulation

Investigations The calcium content of the serum is low except in alkalosis when only the ionized part of the calcium is low the total being normal

Treatment The treatment of tetany depends upon its cause Acid producing salts such as ammonium chloride or calcium chloride in 1 g doses up to 6 or 8 g a day are beneficial when tetany is due to low blood calcium or to alkalosis Frequent convulsive seizures require the administration of anti-convulsant drugs intravenously Once the tetany is under control an attempt must be made to deal with its cause This usually requires the administra tion of vitamin D or its analogue dihydrotachysterol (A T 10) in adequate dosage

Narcolepsy

Narcolepsy is a condition of unknown aetiology characterized by recurrent attacks of an uncon trollable desire to sleep sudden transient loss of tone in the muscles of the extremities or trunk (cata plexy) and pathological weakness of the muscles during emotional reactions such as laughing or crying In the majority of cases the symptoms start without any obvious cause but a few cases may follow acute epidemic encephalitis or head injuries or acute infections such as pneumonia or scarlet fever Prolonged drowsiness or somnolence associ ated with brain tumours cerebral trauma or psy choses should not be described as narcolepsy

There is no known pathological basis to narco *lepsy It occurs four times as frequently in males* as in females The usual age of onset is the second to fourth decade of life though it may begin earlier or later than this

Clinical Picture The attacks of sleep vary in frequency from one to many times daily and in duration from a few minutes to several hours Apparently the sleep is normal in every respect except that it occurs at inappropriate times The desire to sleep can be resisted by great effort but it is usually only temporarily postponed While it often occurs at times conducive to normal sleep such as after heavy meals or sitting relaxed it may overtake a patient at any time such as when driving When the patient desires to sleep he usually seeks bed or chair but occasionally he continues his pre vious activity such as walking while asleep When the patient wakes either spontaneously or after a stimulus which need not be violent he feels com pletely refreshed though he may fall asleep again within a short while He may require anything up to twenty short periods of sleep during the day in addition to a full night s sleep Sleep at night is usually normal though occasionally patients com plain of disturbing dreams

Attacks of weakness and loss of muscle tone which are known as cataplectic attacks are usually associated with some emotional stimulus such as laughter anger fear surprise joy or amusement especially when there is an element of surprise The attack may be so intense that the patient falls help lessly to the ground

Both examination and investigations reveal no abnormalities The E E G is normal during a wak ing period and during the attacks the changes in the E E G are those characteristic of normal sleep

Narcolepsy usually persists throughout life The diagnosis can only be made on the history and is easier if cataplexy is also present

Treatment The tendency to sleep can be relieved in almost all patients by amphetamine sulphate but the cataplexy or lesser attacks of weakness of muscles accompanying laughing or crying are usually not improved The dose of amphetamine sulphate varies from 10 mg to very many times this quantity and the appropriate dose has to be found for each patient The last dose should not be given so late that it prevents nocturnal sleep

Demyelinating Disorders

Loss of myelin occurs in very many neurological conditions including nutritional deficiencies vascular lesions and infectious processes The loss of myelin is only one feature of the pathological process in these conditions and they are not usually included under the heading of demyelinating disorders Another form of demyelination the so called perivascular demyelination is part of the acute encephalomyelitis of the exanthemata There is now increasing evidence that this may be a part of a hypersensitivity tissue reaction in the nervous system This too is generally not included under the heading of demyelinating disorders but it will probably be found to form a pathological link with the diseases described below

Multiple Sclerosis (Disseminated Sclerosis)

Multiple sclerosis is a chronic remitting disorder characterized by numerous areas of loss of myelin in the central nervous system and clinically by a great variety of neurological symptoms and signs There is considerable variation in the symptoms and signs from time to time and as a rule a striking feature of the disorder is the evidence of multiple lesions

Aetiology The cause of multiple sclerosis is unknown though there are many theories These include infection with either organisms or viruses endogenous or exogenous poisons trauma nutritional deficiency and hypersensitivity or allergic reactions This last theory is perhaps supported by the experimental production of demyelination in animals who have been made hypersensitive to certain fractions of the tubercle bacillus There is also suggestive evidence that both initial attacks and relapses of multiple sclerosis are sometimes precipitated by acute infections trauma vaccination and pregnancy Moreover loss of either motor or sensory function confined to one limb developing a week or two after the same limb has suffered various kinds of trauma has been described sufficiently often to suggest that the trauma may determine in which part of the spinal cord a new patch of sclerosis arises

Pathology Minor atrophy in the brain and spinal cord with numerous small irregular greyish areas in the hemispheres particularly the white matter and in the periventricular regions are visible to the naked eye Similar areas are present in the brain stem cerebellum and spinal cord Sections of the nervous system stained for myelin show areas of demyelination in the regions which were obviously discoloured in the unstained specimens and many more plaques very much smaller and often sharply circumscribed may be found scattered throughout all parts of the brain and spinal cord The size of the lesions may vary from tiny pinheads to enormous masses The areas are sharply demarcated from normal tissue Within each lesion there is complete or incomplete myelin destruction with a lesser degree of damage to the axis cylinders and some proliferation of glial cells In older lesions there may be considerable sclerosis

Incidence The incidence of multiple sclerosis varies in different parts of the world In Britain it affects about 1 per 2 000 of the population It is generally more common in temperate climates than in either frigid or tropical regions The incidence in the two sexes is probably equal It develops most frequently between the ages of 20 to 40 but may occur much earlier or later There is sometimes a familial tendency though this varies in different series In Britain it seems to be familial in from 7 to 10 per cent of cases

Clinical Picture Since any part of the nervous system may be affected any neurological symptom is possible A most important feature is the multiplicity of symptoms and their tendency to vary in nature and severity during the passage of time Complete remission of initial symptoms is the rule but as attacks occur with increasing frequency the remissions are less and less complete The usual course varies from 10 to 50 years though the course of a few very acute cases is only a few months.

The onset is usually acute or subacute often with paraesthesias which may be feelings of numbness tingling coldness heaviness or deadness in a limb Sometimes diplopia or loss of vision in one or both eyes is the initial symptom and occasionally it is vertigo which is exactly the same as that of acute labyrinthitis There is no classical form of multiple sclerosis The classical descriptions are of well developed disease in which the manifestations are chronic However an arbitrary anatomical division into the spinal form brain stem or cerebellar form and cerebral form is useful provided its arbitrary nature is remembered and it is realized that many patients have features of more than one form

Spinal Form This is probably the most common type Damage to the posterior and lateral columns may occur initially with resultant paraesthesias in the extremities and weakness or awkwardness of the involved limbs The intensity of these symptoms may vary from day to day and may shift from one limb to another Although weakness is common muscular atrophy is rare except in the terminal stages The

gait is often stumbling or ataxic and there may be partial or complete astereognosis in the hand with awkwardness in performing fine movements Diminution in vibration sense is an early sensory sign Other signs due to affection of the posterior columns such as loss of position sense in the toes develop later Except when a plaque causes an acute transverse lesion of the cord cutaneous sensibility is not usually affected for long or to a great extent

Tremor is frequent At first it may be apparent only in the finger nose finger test but later it may become obvious and continually present preventing the patient from feeding himself or even from sitting upright Urgency and frequency of micturition sometimes with incontinence may occur in the later stages and are usually associated with spastic weakness of the legs Occasionally a well marked spastic ataxic paraparesis develops accompanied by impairment of deep though not usually of superficial sensation

The deep reflexes are usually exaggerated and the plantor responses are often flexor Ankle and knee clonus are common The abdominal responses usually disappear early but the cremasteric reflexes are preserved

Brain stem Form Retrobulbar neuritis resulting in a central scotoma of varying size and visual loss is a frequent mode of onset. The visual loss is much greater than an examination of the fundus would suggest There may be no fundal changes at all though if the plaque of sclerosis is very close to the nerve head papillitis will be seen as shown by redness of the disc and haziness of its margins However severe the visual loss in an initial attack of retrobulbar neuritis normal or near normal vision usually returns in about 2 months though the optic nerve occasionally suffers permanent damage a permanent disabling scotoma being left Further attacks of retrobulbar neuritis may occur with consequent increasing damage to the optic nerve Even though retrobulbar neuritis has apparently cleared up completely evidence of it may be left in pallor of the disc *particularly in the temporal half*

Rarely there is no acute episode but a slow progressive degeneration of the optic nerve accompanied by pallor of the disc

Other ocular disturbances include diplopia which is common initially though often transient and nystagmus impairment of conjugate gaze and pupillary abnormalities all of which are unusual in the early stages Nystagmus is most commonly horizontal though may be vertical In the later stages any abnormality of the pupil may occur

Vertigo accompanied by unsteadiness of gait and nystagmus and sometimes by dysarthria may be the first symptom The nystagmus usually persists after the vertigo has disappeared indicating that the lesion is in the brain stem

Involvement of the trigeminal nerve may result in attacks of what seem to be almost classical trigeminal neuralgia Facial palsies occur sometimes Deafness is rare Pseudo bulbar palsy with forced laughing or crying is a feature of the later stages

Cerebral Form Emotional disturbances are common in the early stages but otherwise cerebral manifestations are usually late Euphoria and other disturbances of mood are characteristic of the advanced disease Convulsive seizures occur in less than 4 per cent of patients Cerebral hemiplegia dysphasia and homonymous field defects are all uncommon In the terminal stages mental deterioration is usual and there may be psychotic episodes

Investigations. During active phases the protein content of the cerebro spinal fluid may be increased to about 100 mg/100 ml Figures higher than this are rare and should lead to a review of the diagnosis A moderate pleocytosis may occur usually with mononuclear cells The colloidal gold (Lange) curve is abnormal in a large number of patients and is usually paretic the precipitation in the first part of the curve being greatest The serological tests for syphilis are negative The other cerebro-spinal fluid constituents are normal

Course and Prognosis The clinical course of the disease is variable but there are usually remissions and exacerbations In about 30 per cent of patients the course is progressive particularly if the symptoms begin after middle age Sometimes the disease is apparently arrested usually with severe residual manifestations after years of relapses and remissions Once the chronic stage has set in the duration is largely dependent upon the nursing care which the patient receives The longer bed sores urinary infection and perforating ulcers can be prevented the longer the patient will survive The very acute cases run a course of a few weeks or a few months

Differential Diagnosis The most important diagnostic criterion is the presence of multiple lesions *disseminated both in the nervous system and in time* When both of these features are present multiple sclerosis is highly probable but even so a careful watch should be kept to confirm that the diagnosis is sustained with the passage of time Apart from this criterion the diagnosis is difficult to reach with certainty As there is no effective therapy the confident diagnosis should not be made until all other possibilities have been excluded if necessary by watching the patient over years Because the possible manifestations of the disease are so numerous the differential diagnosis includes a very great many conditions affecting the nervous system

Treatment Many remedies have been advocated for multiple sclerosis but there is no evidence that any is effective in altering its course Bed rest during acute exacerbations is often advised but is of un certain value and the patient should probably be urged to use his limbs as much as he can Careful re education exercises are of undoubted help in enabling the patient to make the best use of his limbs Even patients who have been regarded as chairbound can sometimes be made mobile by the encouragement and assistance of a skilled physio therapist.

Pregnancy sometimes seems to have an unfavour able effect on the course of the disease and the care of children is certainly a burden to an afflicted mother There are therefore good grounds for dis couraging pregnancy The question of terminating pregnancy is difficult and each case must be con sidered on its merits but when the mother is seriously disabled termination may be justified

Neuromyelitis Optica

This syndrome is characterized by acute retro bulbar neuritis in one or both eyes and transverse myelitis

Loss of vision in one or both eyes due to a retro bulbar neuritis usually precedes the spinal cord involvement by several days or weeks but the con verse may also occur As a rule there is an acute transverse lesion of the spinal cord with a complete flaccid paralysis below the level and absence of all reflexes complete sensory loss and paralysis of th sphincters

Many cases terminate fatally but occasionally there is some degree of improvement without sub sequent development of new symptoms or signs

There is no specific treatment

Schilder's Disease (Encephalitis Periaxialis Diffusa)

This is a rare demyelinating condition occurring most frequently before the age of twenty It affects the hemispheres and may begin in any part of the white matter The signs and symptoms are therefor variable In children epileptic attacks headache vomiting and vertigo are common Cortical blind ness hemianopia and optic atrophy may occur Other manifestations include hemiplegia cortical sensory loss deafness cerebellar and extrapyra midal symptoms and pseudo bulbar palsy Loss of memory dullness irritability euphoria and per sonality changes are always pres nt and confusion disorientation and dementia are usual

Cerebro spinal fluid changes are less common than in multiple sclerosis The condition is usually progressive though the course varies between two or three weeks and some years

Nursing care is the only treatment

Subacute Combined Degeneration of the Spinal Cord

This condition occurs mainly in middle and later life It is associated with pernicious anaemia (p 486) which it may either precede or follow A deficiency of vitamin B_{12} (cyanocobalamin) produces both the megaloblastic anaemia and the changes in the ner vous system

Clinical Picture The description given here is limited entirely to the effects of vitamin B_{12} defi ciency on the nervous system These may be seen in the peripheral nerves the lateral and posterior columns of the spinal cord and the cerebrum

The usual mode of onset is the appearance of paraesthesias in the toes soon followed by the fingers which gradually spread along the limbs There may be sensations of coldness and as though treading on cotton wool This is soon followed by weakness and clumsiness of fine movements

In the commoner flaccid type of the disorder the weakness is mainly peripheral with some muscle tenderness The knee and ankle jerks are lost but fairly soon the plantar responses become extensor Tone is diminished and a glove and stocking type of cutaneous hypalgesia is found Postural sense is also markedly impaired producing a sensory ataxia The spastic type develops as a spastic paresis with hyperreflexia and clonus Flexor spasms may occur and ultimately a paraplegia in flexion may result Every gradation between this and the flaccid type is seen The mental symptoms range from apathy and mental retardation to hypomania and delusional ideas and hallucinations

Diagnosis This has to be made from peripheral neuritis and is dependent on the presence of the signs suggesting cord involvement A histamine fast achlorhydria the bone marrow appearances and the low level of serum vitamin B_{12} confirm the clinical diagnosis

Treatment 1 000 μg of vitamin B_{12} should be given daily for five days followed by 100 μg weekly for three months Thereafter 100 μg should be given every three weeks and reviewed in the light of the blood picture As recovery begins graduated exercises can be started with an attempt at re education The results of treatment depend on the duration of the disorder The peripheral element can be expected to recover fairly well but spinal cord changes are likely to be permanent Folic acid should never be given as it worsens the n urological condition

CHAPTER 18

Diseases of the Kidney

CHRISTOPHER HARDWICK

In 1827 Richard Bright physician to Guy s Hospital described the clinical features and morbid anatomy of patients dying with dropsy and albuminuria thus laying the foundations of our modern knowledge of diseases of the kidneys Before this time the occasional occurrence of dropsy with albuminuria was recognized and it was known that in some of these cases the kidneys might be abnormal No description of the appearances of the kidneys in these diseases had been given and it was not appreciated that when there was oedema and albuminuria the kidneys were always abnormal

During the nineteenth century the descriptive science of morbid anatomy became pre eminent and correlation was made between the clinical picture of the disease during life and the appearance of the kidneys at post mortem so that numerous classifications of renal diseases were made It was in this period that such terms as large white kidney secondary contracted kidney and flea bitten kidney were commonly used

More recently with the elaboration of modern techniques in biochemistry together with advances in microscopy it is becoming apparent that symptoms and signs in renal disease are not due so much to damage and distortion of the kidney as a whole as to damage to a particular part of the nephrons As the complexities of the processes by which urine is excreted are understood so it is realized that structural damage is not the only way in which renal disease may occur Biochemical processes may be deranged without any structural change and conditions such as salt losing nephritis potassium losing nephritis and even water losing nephritis have been described

Nephritis however is not the only type of disease of the kidneys which we must consider There may be congenital anatomical abnormalities acute and chronic infections degeneration and stone formation Finally the frequent occurrence of hypertension when the kidney is damaged means that possible renal causes of hypertension will have to be considered as well as the effects which a raised blood pressure may have on the kidneys

Renal Function and its Estimation

The kidneys carry out their two functions of excreting waste products and maintaining the biochemical balance of the body by filtering the plasma from its protein content through the glomeruli and by the absorption from this filtrate of such fluid and electrolytes by the tubules as are required by the body At the same time some substances are added to the urine by active secretion by the tubules

Although the daily output of urine is only 1½ litres the amount of glomerular filtrate formed each day is 180 litres—a volume sufficient to give three warm baths! Again whereas the daily output of sodium is 6 g the glomerular filtrate contains a hundred times this amount nearly all of which has to be re absorbed by the tubules In other words 1½ lb of common salt must be put back into the circulation by the tubules Seen in this light the most striking feature of renal function is not the excretion of 1½ litres of urine to the exterior but the secretion of nearly 180 litres of fluid into the circulation This helps to explain the paradox that when renal failure occurs the amount of urine produced may be greatly increased only a slight impairment of tubular re absorption leading to a great increase in the volume of urine

All this work is carried out by the nephrons which are tiny tubules 3 cm in length and 60μ in diameter at their greatest point The processes involved include simple filtration absorption by osmosis and secretion in both directions across the walls of the tubules Control of all these mechanisms is an equally complicated process and is effected by hormones and by nervous impulses

Thus it will be seen that the efficiency of the

kidneys may be affected in many different ways The controlling mechanism may be at fault the pressure required for glomerular filtration may be lacking the walls of the tubules may be damaged or the various secreting systems may be deranged Conversely the kidneys may be damaged without there being any upset of their working capacity as in neoplasia or tuberculosis

Although the accurate measurement of any one of the intricate processes involved in the secretion of urine may be impossible it is possible to measure the overall efficiency of the kidneys We *can* determine how well the kidneys are carrying out their jobs of getting rid of waste products and of maintaining the equilibrium of the body fluids

One of the characteristics of renal function in health is the ability of the kidneys to secrete urine of high or low specific gravity as the occasion demands In hot weather or when fluid is withheld a small volume of urine with a specific gravity between 1 025 and 1 035 may be passed On the other hand in cold weather or when much liquid is drunk a large volume of urine with a specific gravity in the region of 1 002 is passed When the kidneys are damaged they lose this elasticity of function and the range of the specific gravity of the urine passed becomes narrowed progressively until finally all urine passed has a specific gravity of 1 010 which is the specific gravity of protein free plasma

Tests can be elaborated to demonstrate this impairment of function But before these are described it should be realized that some idea as to the extent of the damage can be obtained from a consideration of the patient s history If the power of concentration is lost then in order to eliminate a given quantity of solutes a large volume of water must be voided by the kidneys This increase of urinary output will be most noticeable during the night and nocturnal frequency may be an early symptom of renal failure

The Concentration Test

Method On the evening before the test is to be carried out the patient is given a supper rich in protein but without anything to drink Any urine passed during the night is discarded At 8 a m the patient passes urine and this specimen and two subsequent ones passed at 9 a m and 10 a m are saved and the specific gravity of each is estimated For this purpose a sensitive urinometer with a large scale reading between only 1 000 and 1 030 should be used so that an accurate determination can be made The conventional instruments which have a relatively small scale reading from 1·000 to 1 060 make an accurate reading impossible If the urine contains much albumen a correction will have to be made by subtracting 0 003 for each gramme of albumen per 100 ml of urine Of the three specimens obtained in this test the specific gravity of at least one should be above 1 020 In health figures much nearer to 1 030 will be obtained so that failure to reach the arbitrary figure of 1 020 denotes a very definite impairment of renal function

The Dilution Test

This test examines the ability of the kidneys to eliminate a large draught of water soon after it has been drunk To do this the water must of course reach the kidneys so that if the body is waterlogged with oedema or if the circulation is poor as in cardiac failure the patient may give a poor performance in the test even though the kidneys themselves may be undamaged

Method To perform this test the patient should be in bed If possible it should be carried out immediately upon waking for then the patient will be under basal conditions and in particular will not have had anything to drink which could act as a diuretic (such as tea or sweetened fruit juice) in the four hours before The patient empties his bladder and the specimen is discarded in the succeeding half hour he drinks 1 200 ml (2 pints) of water At the end of each hour after this for four hours a specimen is collected and the volume and specific gravity of each is measured In the normal subject the total volume passed in the four hours is over 1 000 ml and the lowest specific gravity of the four specimens is 1 002

It is sometimes recommended that the concentration and dilution tests should be carried out consecutively on the same day This is unwise if only because in such circumstances the patients must be kept under conditions of test for seven hours

Clearance Tests

If a substance occurs in both the blood and the urine it is a simple matter to calculate how much blood would be required to provide the amount of the substance which is contained in a given volume of urine If U mg/100 ml is the concentration of a certain substance in the urine and V ml is the volume of urine passed in one hour then $\frac{U \times V}{100}$ is the amount of the substance excreted If P mg/100 ml is the concentration of this same material in the plasma then the volume of plasma that would be required to furnish the amount $\frac{U \times V}{100}$ will be $\frac{U \times V}{P}$ ml Note that this last quantity is a hypothetical one It is not the amount

of blood which does in fact provide the substance in the urine but it is the volume of plasma that would be required if it was completely cleared of the substance

This fraction $\frac{UV}{P}$ is known as the clearance of a substance Most commonly we talk of urea clear ance for urea is easily measured in both plasma and urine but the principle can be applied to any substance in the blood which is excreted by the kidneys In recent years the scope of clearance tests which were first introduced by van Slyke in 1928 has been considerably widened by a study of the clearances of foreign substances introduced into the blood For this purpose the material has to be introduced directly into the blood stream at a steady rate and the bladder must be emptied completely by catheterization and lavage Such tests are there fore impracticable for the routine assessment of patients but by the use of substances such as inulin diodine and para amino acid a great deal has been learnt of the physiology of the kidney

Method For the estimation of urea clearance no special preparation of the patient is required but the common diuretics such as tea and coffee should not be taken immediately before At the beginning of the test the patient should empty his bladder and the specimen be discarded. One hour later urine is voided and the volume and urea content of the sample are measured After a further period of one hour a second specimen is obtained and is similarly analysed At some time during the test blood is taken and its urea content measured The maximal clearance $\frac{U \times V}{P}$ is then calculated for each period and the results compared with normals for patients of similar height and weight and this is expressed as a percentage of the normal

When the rate of the secretion of urine is low—less than 2 ml/min—then the rate of the secretion of urea is proportional to the square root of the volume of urine and the formula becomes $\frac{U}{P} \times \sqrt{V}$ This is known as the standard clearance

The interpretation of the results of urea clearance tests as in all laboratory procedures which translate a disease process into mathematical symbols de mands care An isolated estimation does not carry a great deal of significance—a clearance of 50 per cent of the average normal does not mean that half the kidney is destroyed Serial readings are however of value for changes do follow the clinical course of a nephritic process closely Again the urea clearance test by itself is of no help in the diagnosis of a case of nephritis and it may be of little help in assessing the prognosis For example although two patients with renal disease may have identical values for their urea clearance one may have had an acute illness while the other patient may have been ill for years

Dye Tests

The excretion of dyes such as phenolsulphon phthalein indigocarmine and methylene blue pro vide simple visual tests of renal function The accu rate estimation of the amount of dye eliminated in a given time provides a quantitative measurement of renal function On the whole the results of such tests are uncertain and they have little advantage over van Slyke s urea clearance test so that they are not commonly used in this country

Dyes are however very useful at cystoscopy Then both ureteric openings can be seen and the time taken for dye which has been injected to appear at either orifice gives a good indication of the over all renal function Delay in the appearance of the dye on one side suggests considerable impairment on that side

Radiology

Intravenous pyelography will not only outline the kidney but the intensity of the shadow is some measure of the efficiency of the organs More recently it has been found possible to inject radio opaque dyes directly into the aorta above the site of the renal arteries or by a polythene tube intro duced into the renal arteries by way of the femoral vessels By this means the vasculature of the kidneys can be outlined in good pictures both the glome rular and tubular vascular networks can be dis tinguished

Blood Chemistry

When renal disease is severe alterations in the blood chemistry will occur if the kidney cannot maintain the chemical equilibrium of the body For a long time it was thought that the principal change was in the urea content of the blood which rises with renal damage and so this condition was known as uraemia Although usually progressive in many cases the concentration of the constituents of the blood becomes fixed at a new level and a state of chronic uraemia or compensated renal failure occurs which may persist for many years

While the level of the blood urea (normal 20–40 mg/100 ml) is to some extent a measure of the severity of renal disease it is the changes in other constituents which may determine the symptomatology The alkali reserve (normal 22–27 mEq/1 50–60 vol per cent) is reduced

when renal failure occurs Sodium may seem to be normal (136–145 mEq/l) in the circulating blood stream but may be retained in the tissues causing oedema In the rare cases when there is excessive sodium loss a clinical picture similar to that of Addison s disease may be produced When there is sodium retention the potassium (3 5–5 0 mEq/l) may be reduced causing apathy anorexia and vomiting A low blood calcium (8 5–10 5 mg/100 ml) will cause muscular irritability and tetany

Abnormalities in the Urine

Proteinuria A minute quantity of protein normally occurs in the urine The amount is however so small that it cannot be detected by the usual test of coagulation by heat and the addition of acetic acid Albuminuria is said to occur when protein is demonstrated by this test Strictly speaking both albumen and globulin may be present though the former is always in excess

Increased amounts of protein may be found in the urine of normal subjects after violent or prolonged exercise and in extremes of temperature and in certain young people of asthenic build In fever there may be albumen in the urine which disappears as recovery takes place leaving no evidence of renal impairment

Orthostatic albuminuria is the name given to the condition in which protein appears in the urine of young subjects of poor physique Characteristically the urine is free from abnormality when the patient is lying down at rest but albumen appears after activity This is a benign condition but as the finding of albumen in the urine is usually of serious import very strict criteria must be observed before the diagnosis of orthostatic albuminuria can be accepted The patient must be below the age of 25 Males are more commonly affected than females The physique must be indifferent that is the weight must be below the average for the height the musculature of poor tone so that the patient stands badly with round shoulders and an exaggerated lumbar kyphosis A specimen of urine passed immediately on waking must be free from albumen After exercise a small quantity of albumen may be found but the centrifuged deposit of the urine must show no casts and renal function tests must be normal Finally there should be no history of previous renal disease Although there is no reason why a patient who has had a nephritis in childhood should not develop orthostatic albuminuria in later life it is probably wiser in such cases to regard the albuminuria as evidence of a continuation of that disease and not to make the diagnosis of orthostatic albuminuria

When there is disease of the kidneys the quantity of albumen in the urine may vary from a faint trace to as much as 5 per cent Accompanying it there may be casts in the urine which can be demonstrated in the centrifuged deposit of a fresh specimen As their name suggests these are cylindrical masses of protein bearing the imprint of the tubules where they are formed

Hyaline casts are translucent bodies which occur in the urine of healthy subjects especially after exercise They are also found when there is renal disease but because they can occur in the absence of disease no significance can be placed on their appearance Epithelial and granular casts on the other hand are formed in the tubules by the disintegration of their lining they are therefore always indicative of active renal disease When blood or pus are in the urine red or white cells may be condensed together to form blood or pus casts

Inflammation in the Renal Tract

The Importance of Congenital Abnormalities

Infection of the kidneys and the urinary tract by bacteria especially *E coli* is a common happening Organisms of all kinds must enter the blood stream in small numbers far more frequently than we realize Bad teeth infected tonsils and the bowel as well as foci such as boils and infected cuts may all be responsible That these organisms do not cause illness more often is due to the highly bacteriostatic action of the blood and to the rapidity with which they must be excreted by the kidneys Normally these bacteria do not have time to multiply while they are in the renal tract If however there is any obstruction to the flow of urine organisms can establish themselves and a urinary infection will occur

A congenital abnormality is a frequent cause of such stasis In persistent or relapsing cases particularly such a lesion must always be suspected The malformation may occur in the urethra the bladder the ureters or the kidneys themselves Sometimes

the fault may lie outside the renal tract as when an aberrant renal artery presses upon the pelvis of the kidney In time this becomes dilated and the condition of hydronephrosis is produced In polycystic disease both kidneys are converted into masses of cysts The enlargement may be considerable so that they can usually be easily felt Symptoms may be caused by the rupture or infection of a cyst with abscess formation by the development of hypertension or by renal failure The condition is often familial and may be associated with similar cyst formation in the liver or lungs

According to whether the brunt of the disease occurs in the bladder the renal pelves or the kidneys themselves so we speak of cystitis pyelitis or pyelonephritis It must be remembered however that there is no barrier to the spread of organisms from one part of the urinary tract to another and therefore although clinically the illness may seem to be an acute cystitis in practice there will be infection of the kidneys and ureters as well

In addition to *E coli* streptococci staphylococci *Proteus Ps pyocyaneus* as well as the organisms of tuberculosis and typhoid fever may be implicated Normally the organisms enter the renal tract by the blood stream but in females the shortness of the urethra and its closeness to the anus provides another portal of entry In pregnancy the gravid uterus compresses the ureters particularly where they cross the pelvic brim Because of these features acute infections of the urinary tract occur most commonly in females

Clinical Picture The illness begins abruptly and a rigor may occur in adults In children there may be a convulsion and this is one of the causes of fever in the newborn Except in the young and the elderly in whom there may be high fever constitutional upset is minimal Pain and frequency of micturition are usually the leading symptoms but may be absent Haematuria is not uncommon and may be profuse Pain may occur over the bladder in the suprapubic region or in one or other renal angle

There may be tenderness in the suprapubic region or in one or other renal angle The urine which is strongly acid becomes turbid and has a characteristic smell of decaying fish Under the microscope mobile organisms may be seen

Treatment Symptomatic relief can be quickly obtained by giving potassium citrate in sufficient quantities to render the urine alkaline A mixture containing 4 g (60 gr) can be given every 2 hr until a specimen turns litmus paper blue the dose can then be given 4 hourly

Esch coli are sensitive to sulphonamides and this is the treatment of choice Sulphafurazole 2 g initially followed by 1 g every 6 hr until the temperature has been normal for 48 hr or a total of 30 g has been given is a satisfactory drug Sulphamethizole 0 2 g q d s or sulphadimidine 3 g initially followed by 1 g 6 hourly may also be used Copious fluids at least 5 pints a day should be given

A resistent organism or a mixed infection should be treated with the appropriate antibiotic This will have to be determined by sensitivity tests in the laboratory which will entail a delay of two or three days before starting treatment In the absence of such tests streptomycin is the best drug to use A short course only is required 0 5 g twice daily for 3 days is usually sufficient.

A single attack of a urinary infection in a male calls for a full urological examination with an intravenous pyelogram and possibly cystoscopy and retrograde pyelography In women a single attack does not indicate a renal abnormality nearly so strongly If however the attack proves resistent to treatment or soon relapses or recurrent infections occur at short intervals or if pain in one or other renal angle persists then full investigation is required

The same rules hold for attacks of urinary infection in children The younger the child the more likely is it to have a congenital abnormality of the renal tract It is however unwise as well as impracticable to subject every child who has such an infection to intravenous pyelography and cystoscopy In the very young therefore the illness should be treated with alkalis A 6 months old infant can be given 4 g (60 gr) each of potassium citrate and sodium bicarbonate in divided doses in a mixture in a day If the urine is kept alkaline in this way it will become sterile within a week If it fails to do so or a relapse occurs then a sulphonamide can be given and such cases can be selected for full investigation

Renal Calculi

This is a subject which is fully dealt with in surgical textbooks The medical aspects however require some consideration In addition to the part they play in precipitating and prolonging urinary infections renal calculi may cause pain or haematuria or they may be evidence of an inborn error of metabolism

Pain may be of two sorts There may be a con

stant backache which is especially severe in one or both renal angles This occurs with large stones which obstruct the flow of urine from the pelvis of the kidney and so cause hydronephrosis Small stones and crystals particularly those of oxalates may give rise to renal colic as they pass from the renal pelvis into and along the ureters This severe spasmodic pain may start in one loin and then radiate to the groin The patient sweats becomes pale and may vomit

Haematuria accompanies or may follow the attack of renal colic It is usually sufficient to be obvious to the naked eye but it may be only micro scopical or even absent Some clue to the cause of the haematuria may be given by the microscopic examination of the centrifuged deposit of the urine This may reveal the characteristic whetstone or barrel shaped crystals of uric acid or the envelope crystals of calcium oxalate Cystine is an amino acid containing sulphur which appears as hexagonal plates Its presence in the urine is due to an inborn error of metabolism as described originally by Gar rod Cystine crystals and calculi may form in young patients and may be repeatedly formed during life Infection will determine the occurrence of stones in some members of a family and not in others even though they all have the same inherent defect

From the physician s point of view the occurrence of renal calculi may be important as an indication of an underlying disorder of the parathyroid glands (*see* p 150) In primary hyperparathyroidism the level of calcium in the blood is raised and the amount of calcium in the urine is increased The formation of stones of calcium carbonate will then easily follow and indeed there may be calcification in the renal tubules themselves In certain types of chronic renal disease the kidney may be unable to excrete ammonia fixed base therefore appears in the urine and to maintain the acid-base equilibrium in the body calcium salts may be utilized To do this the parathyroids hypertrophy Calcium is with drawn from the skeleton and the high level of ionizable calcium in the blood may lead to meta static calcification in the soft tissues as well as to stones in the kidney The large parathyroid glands are thus associated with the paradoxical condition of osteoporosis with calcium in the soft tissues par ticularly in the walls of the arteries and renal cal culi Calcified vessels in a pelvic X ray almost always indicate chronic renal disease

Bright's Disease

This old fashioned term is used to describe all those renal disorders in which there is both disease of the kidney substance and disorder of its function It is preferred to the term nephritis as this is now so often used as a synonym for glomerulo tubular nephritis that it does not have a wide enough con notation to include all the many disorders which may cause renal impairment

An elaborate classification of the underlying causes of Bright s disease often confuses rather than helps the clinician Founded as they are on morbid anatomy such classifications suggest that disease is a static and not a progressive and a varying process For instance one patient with glomerulo tubular nephritis may die because of extensive renal damage but before this stage has been reached an other patient may die of heart failure while a third may die from a cerebral haemorrhage In each case the kidneys will have a different appearance at autopsy and the morbid anatomist may be tempted to put them in different groups in his classification

In place of some conventional classification three types of renal disease will be described These are acute glomerulo tubular nephritis the nephrotic syndrome and renal failure

Acute Glomerulo tubular Nephritis

This disorder may affect individuals of any age but is more common in children and young adults There is a close connexion between it and strepto coccal infections for in most cases an attack of tonsillitis or scarlet fever precedes the onset of renal symptoms by a few days or a few weeks

Clinical Picture The symptoms begin gradually There may be headache malaise fever and vomit ing Aching in the back and loins is common Bloody urine may be the first indication as to the nature of the illness especially in children The quantity of urine is diminished and in severe cases there may be anuria Oedema may be prominent characteristically the face may be noticed to be puffy in the mornings and the ankles become swollen in the evenings

On examination the patient appears to be pale and is febrile and pitting may be demonstrated in the ankles the sacral pad or in the face The diastolic blood pressure may be moderately raised and occasionally this increase may be sufficient to embarrass the heart so that moist sounds occur in the lungs There may be tenderness in one or both

renal angles The urine always contains albumen and usually blood in sufficient quantities to make it appear smoky red cells can be seen in the centri fugal deposit which in addition will contain cellular casts

Laboratory studies show an anaemia owing to the hydraemia or increase in body water that occurs There may be nitrogen retention the blood urea being raised to about 50 or even 100 mg/100 ml Renal function tests will be impaired

The favourable outcome of the disease and its relatively short course differentiate it from most other renal diseases In acute pyelonephritis organ isms can be demonstrated in the urine and there is no oedema The haematuria from a papilloma of the kidney or bladder is not associated with any constitutional upset.

In children haematuria may be profuse and the disease is short and recovery seems to be complete To this variant of the disorder the name acute haemorrhagic nephritis has been given

Treatment The aim of treatment is to rest the kidneys and to give the nephrons as little work to do as possible until recovery has set in The patient should be nursed in bed until the acute illness has subsided As long as the urinary output is dimi nished so the quantity of fluid given by mouth should be curtailed and 600 or 1 200 ml (1 or 2 pints) should be allowed this should consist entirely of fruit drinks No protein at all should be given the patient being allowed only fruit This strict régime can be kept up until the output of urine increases or for about 5 days After this time there is likely to be a breakdown of tissue proteins so that a small quantity of proteins 40–50 g should be allowed As recovery takes place so the diet and activity can be increased

In severe cases when there is anuria vomiting and considerable nitrogen retention the measures to be de cribed under the treatment of acute renal failure should be adopted

The Nephrotic Syndrome

In this condition there is impairment of renal function with great and persistent oedema gross albuminuria and a raised cholesterol content of the blood There are a variety of causes and these include subacute glomerulo tubular nephritis chronic pyelonephritis diabetic nephrosclerosis polyarteritis nodosa systemic lupus erythematosus amyloid disease (which may be primary or secon dary to chronic suppuration) and renal vein thrombosis

Clinical Picture In each example the clinical picture is identical and there may be no clue to the true nature of the condition There may however be a history of previous urinary infections or the patient may have been a diabetic for many years In polyarteritis nodosa and systemic lupus erythema tosus there may be a history of previous rheumatic like diseases other systems may be affected and investigations will show an exceedingly raised ery throcyte sedimentation rate and in the latter disease the L.E cell phenomenon may be demonstrable in the blood

The symptoms of the nephrotic syndrome begin insidiously and may be present for some time before medical advice is sought Oedema is always present at first there may be only slight swelling of the ankles noticeable in the evenings or there may be puffiness around the eyes in the mornings This in creases and becomes massive and generalized and there may be pleural effusions The general distribu tion of the oedema in renal disease distinguishes it from the oedema of heart disease which spares the face and is greatest in the most dependent parts It must be emphasized however that in both dis eases the oedema is related to sodium retention The different distribution of the dropsy is due to mechanical causes—the patient with renal disease can lie flat and so the swelling is generalized on the other hand cardiac patients cannot lie flat but have to sleep propped up in bed and so their faces are spared and the fluid collects in the most depen dent parts

As their disease progresses the patients begin to feel ill They become tired and listless their appe tites become poor and they have nausea and may vomit Usually they are thirsty their mouths be come dry and may be foul tasting The urinary out put is maintained and may even be increased despite the oedema Nocturia is a common symptom

On examination the patients are seen to be pale and have a generalized dropsy The pulse will be rapid and if the blood pressure is very much raised the heart will be enlarged Pleural effusions may be present The tongue will be furred and there may be ascites The urine which will be dilute contains a large quantity of albumen (2 per cent or more) hyaline and granular casts can usually be seen

Investigations Laboratory studies confirm the presence of anaemia which is usually of the hypo chromic microcytic variety Renal function tests will be impaired and the blood urea may be raised The plasma proteins are always reduced the albumen is especially affected and there may be a relative increase of the globulin fraction This lowering of the albumen is due to the heavy albuminuria and it has been thought that the consequent drop in the osmolarity of the plasma is responsible for the production of the oedema This is only partly true for it is now possible to get rid of the oedema by

the appropriate treatment and provided these measures are continued then the oedema does not recur even though *the plasma albumen remains at its* previous low level The serum cholesterol is always raised

The nephrotic syndrome is a grave condition and *in most cases it proves fatal* within 1 or 2 years whatever may be the underlying cause A spontaneous remission of the oedema and in children of the albuminaria as well may occur In children such a recovery though rare may be complete but in adults this does not happen although the remission may last for as long as 15 years This is particularly so when the underlying cause is subacute glomerulo tubular nephritis

Although the history and clinical picture may give no reliable clue to the exact diagnosis of the disease responsible for the nephrotic syndrome it is now possible to learn the nature of the true pathology by means of a needle biopsy of the kidney Details of this procedure can be found in current medical literature and will not be described here the operation should be carried out by some one who is experienced in the technique To know the exact diagnosis is an obvious advantage in directing the treatment of any condition this is certainly true of the nephrotic syndrome and if possible a needle biopsy should be carried out in every case

Treatment Until his condition has been brought under control a patient with the nephrotic syndrome should be nursed in bed In the early stages his fluid intake should be restricted to sufficient to allay *thirst*

Treatment is directed particularly at controlling the oedema So often this is the disabling feature—the grossly swollen ankles prevent the patient wearing any *shoes or even prevent him from walking* If it can be reduced the patient can often return to work very successfully despite his impaired renal function There are five methods that may be tried namely *diet ion exchange resins diuretics steroids* and mechanical methods

A low sodium diet is the sheet anchor in the treatment of this and of all general oedematous *states A ban on the use of salt in cooking* as well as at the table is insufficient and precise instructions should be given about the choice and preparation of a diet containing only 500 mg of sodium a day *In its extreme form* such a diet *may* consist of tinned fruit and boiled rice only but most patients are unable to take *such an* unpalatable menu for long and a more appetizing regimen is given on page 480

A high protein diet of about 150 g has been recommended in the nephrotic syndrome in an endeavour to increase the quantity of the plasma protein When there is no nitrogen retention such a diet may be given but its effect upon the proteins is disappointing Meat and meat extracts contain a good deal of salt and as far as relief of oedema is concerned the bad effect of this more than counter balances any good that may come from an increase of the plasma proteins

When the kidney is damaged the use of diuretics substances which increase urinary output by their direct action on the nephrons must clearly be limited They may easily do more harm than good This is particularly true of the mercurial diuretic mersalyl which acts on the tubules interfering with the resorption of water Though it has been used with success in this syndrome it usually causes an increase in the albuminuria and in the casts in the urine More useful is chlorothiazide (Saluric) a non mercurial diuretic The dose is 1 g twice daily 2 or 3 times a week The drug causes an increased excretion of potassium and if given over a long period foods such as tinned fruit which are rich in this mineral should be given In some cases potassium chloride 1 g t d s may be required Acetazolamide which is known to inhibit carbonic anhydrase may also be effective Single doses of 250 mg should be given at weekly intervals by mouth If given more frequently it seems to lose its potency

Ion exchange resins are substances which contain *anions or cations in loose combinations* and which can give up these ions for others under certain conditions For the treatment of oedema a synthetic resin polystyrene sulphonate containing am*monium and potassium is used* In its passage through the intestines this substance picks up sodium ions in exchange for its ammonium and potassium ions As a result there is less sodium *absorbed from the intestines* and the body is thus depleted In consequence the tissues can no longer *hold water and so oedema disappears The dose* of ion exchange resin is *15 g/day and the granules should be sprinkled* into a tumblerful of fruit juice and quickly swallowed

Steroid therapy usually results in the patient retaining water Nevertheless *both* A C T H and cortisone have been used with success in the nephrotic syndrome It seems that short interrupted courses are often followed by a copious diuresis when the drug is withdrawn Continuous treatment with small doses of cortisone (1–2 mg/kg body weight) is more effective Prednisolone which has less sodium retaining properties may be given in large doses until improvement sets in *In adults* 200 mg may be given and in children 60 mg daily When the desired effect has been obtained the *dose* is slowly reduced

Richard Bright wrote in 1836 'There is another mode of depletion which though it may at first appear but a temporary and mechanical expedient I am by no means disposed to leave out of con sideration I mean the discharge of the fluid from the cellular membrane where anasarca exists by punctures To day this long established method re mains one of the most certain ways of relieving oedema After the introduction of the method by Bright various improvements of the technique were devised—all had the effect of increasing the likelihood of infection in the subcutaneous tissues and so the method fell into disrepute Most notorious in this respect are Southey s tubes which are small trochars and cannulae which have to be pushed without anaesthetic far into the sub cutaneous tissues parallel with the skin The bar barous nature of this operation has also added to the discredit of the method

With a careful aseptic technique and modern antibiotics there is now no risk of infection especi ally if a simple technique as advocated by Bright is used The patient should be nursed in a chair or a cardiac bed for 2 or 3 days Then after thorough cleaning of the skin three incisions each no more than ½ in long should be made through the full thickness of the skin on the dorsum of each foot The feet are then covered with a mass of dry dress ings wool and sterile towels The whole soon becomes soaked and will require frequently chang ing which must always be done with the strictest aseptic technique

Renal Failure

Uraemia is the name given to the condition which is produced when the kidneys are so damaged that they are unable to carry out their work effectively Either or both of two things then happen Waste products may accumulate in the body and/or the isotonicity of the blood and tissue fluids may be affected These changes will occur irrespective of the nature of the underlying disease and the clinical picture produced depends not upon the type of the disease but upon the speed with which the body s biochemistry is upset Thus we recognize two ill nesses acute and chronic uraemia

Acute Uraemia

In its simplest form this is the condition which occurs when a stone becomes impacted in one ureter the other kidney and ureter having been previously removed There are however a variety of other causes of *acute uraemia in many* of which the mechanism of production of symp toms remains obscure Though the syndrome has been recognized for many years it was the Battle of Britain and the blitz which brought it into prominence and so stimulated research into its occurrence pathology and treatment It was as the Crush syndrome that it was then known When the air raids on this country were in progress physicians began to recognize an apparently new clinical entity An individual would be trapped in a bombed building by fallen masonry lying across his body and legs While the rescue parties dug him out he remained cheerful and uncomplaining when finally released he was often found to have no more injuries than severe bruising Nevertheless on re-moval to hospital his condition deteriorated and in about 4 days he was dead The most striking feature of the short illness was an almost complete anuria Later in the war a similar condition was noticed to follow severe wounds and was called traumatic anuria It was then realized that this form of uraemia might accompany a variety of conditions these include mismatched blood transfusions sul phonamide sensitivity Addison s *disease alkalosis* and diabetic coma A similar state may occur after concealed antepartum haemorrhage and other obstetrical emergencies and after major operations and injuries of any kind

It seems that the essential precursor of acute uraemia is a period of shock with extreme hypo tension lasting some hours

Clinical Picture A patient with acute uraemia looks grey with parched tongue and dry inelastic skin In addition to the anuria vomiting is frequent and hiccoughs may be troublesome There is usually no headache and consciousness may not become clouded even though the blood urea rises to nearly 1 000 mg/100 ml When these great concentrations are reached the skin may be covered with a fine white powder This deposit of urea is known as uraemic snow

In addition to the very high levels of the blood urea there is a lowering of the chlorides in the blood and of alkali reserve The potassium may be in creased and in some patients this may cause ven tricular fibrillation and death Any urine that is passed may be highly pigmented but its specific gravity is fixed between 1 014 and 1 018 Despite the very high and increasing blood urea the con centration of urea in the urine is low and is usually less than 2 per cent The urine is always highly acid and attempts to make it alkaline are unavailing

Pathologically in the obstetrical cases there is necrosis of the cortex of both kidneys—acute cortical necrosis Thus an important region con *taining most of the glomeruli is wiped out and so* recovery is not to be expected

In all other cases however it is not a whole area of the gross anatomy of the kidney that is wiped out

the appropriate treatment and provided these measures are continued then the oedema does not recur even though the plasma albumen remains at its previous low level The serum cholesterol is always raised

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Treatment is directed particularly at controlling the oedema So often this is the disabling feature—the grossly swollen ankles prevent the patient wearing any shoes or even prevent him from walking If it can be reduced the patient can often return to work very successfully despite his impaired renal function There are five methods that may be tried namely diet ion exchange resins diuretics steroids and mechanical methods

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uncommon The tongue is dry and furred the breath is foul smelling and a uriniferous odour may be detectable The peripheral arteries are thickened and tortuous and the blood pressure is almost always raised Pulsus alternans may be present The heart is enlarged and there may be an apical gallop rhythm a grave sign Pulmonary oedema may provide further evidence of left ventricular failure Abdominal examination is usually negative but polycystic kidneys or a large hydronephrosis may be felt and gross constipation may produce an easily palpable colon The tendon reflexes may be exaggerated and there may be signs of tetany There may be a severe hypertensive retinopathy with exudates haemorrhages and finally papilloedema

Investigations The urine always contains albumen though the amount may be small it is dilute and as the patient s condition worsens so its specific gravity becomes fixed at about 1·010 Anaemia is always present it is microcytic or normocytic The blood urea is raised but the amount of this does not necessarily reflect the severity of the renal damage If the disease is progressing rapidly then there may be uraemia with only a moderate rise of the blood urea If however the disorder is protracted then the nitrogen retention will occur only very slowly and extremely high levels of blood urea may occur with very little constitutional disturbance The alkali reserve is usually decreased

Important changes may occur in the levels of the electrolytes of the blood In some cases these may dominate the clinical picture to such an extent that the underlying renal failure may not be appreciated Thus in the so-called salt losing nephritis in which sodium is lost the clinical picture may be confused with Addison s disease In the Fanconi syndrome there is an upset in the way in which the kidneys handle phosphate sugar and amino acids

Treatment. This must be symptomatic and palliative rather than curative By the time the patient becomes uraemic the kidneys are almost completely destroyed so that recovery is not to be expected For this reason temporary expedients such as the artificial kidney or dialysation have little place However effective they may be such measures will give only temporary relief and they cannot affect the hypertension or the anaemia Nevertheless something can be done to buttress the failing renal function and to relieve the patient s suffering

Severe cases should be in bed and removal to a hospital where both nursing and laboratory facilities are available may be necessary In the early stages and in mild cases such a move is not necessary and although heavy work is impossible many uraemics can still attend at their office and do very useful work The diet must be low in its protein content about 40 or 50 g if there is oedema the sodium intake will have to be low 500 mg In the absence of anasarca a large fluid intake is essential 4–5 pints may be required each day The aim is to ensure a maximum volume of urine To ensure this the patient may be provided with a large Winchester bottle with graduations in pints painted on it. He should be instructed to drink sufficient to fill it to the 5 pint mark every day In advanced cases when anuria supervenes the fluid intake must be reduced and if intravenous alimentation is used care must be taken to see that the circulation is not overloaded An amount equal to one litre plus the volume of the previous day s urine only should be given An attempt to make good any deficiencies in electrolytes can be made by giving the appropriate substance and the acidosis can be dealt with by using intravenous sodium lactate solution

The anaemia fails to respond to any of the usual haematinics Iron both by mouth and intravenously achieves little The same is true of liver extract cyanocobalamin and folic acid Transfusions of fresh blood will give temporary improvement they must always be given very slowly so as to avoid overloading the circulation

The hypertension is best left untreated unless there is evidence that the patient is standing up badly to it Papilloedema hypertensive cerebral attacks and acute pulmonary oedema are all indications for the use of hypotensive drugs as are signs such as an apical gallop rhythm or pulsus alternans Hexamethonium bromide by injection is the most reliable preparation to use Other preparations such as reserpine and pentolinium are uncertain in their action and may be toxic After a test dose of 25 mg of hexamethonium bromide treatment can be started by giving 50 mg twice daily As tolerance is developed so the dose can be steadily increased

Mecamylamine is a ganglion blocking agent which is effective by mouth in small doses Beginning with 2 5 mg twice a day the dose can be slowly increased until a satisfactory drop in the blood pressure is obtained As with similar drugs constipation may be a troublesome side effect but more serious toxic manifestations are unusual The use of this drug in cases of nephritis may be dangerous for with a drop in blood pressure renal function may be impaired A careful watch must therefore be kept on the urinary output particularly in the early stages of treatment

Symptomatic measures will include mouth washes to alleviate the foul taste in the mouth Analgesics such as tab codeine co and even pethidine will relieve the headaches Venesection is indicated for severe hypertension if the patient is not too anaemic Lumbar puncture is needed for cerebral

but damage is done to a particular part of some or all of the nephrons The tubules become necrotic and the epithelium lies loose in the lumen together with other debris such as crystals of sulphonamide In places the tubule wall may rupture into the venous spaces—which may account for the very high levels of the blood urea which are characteristic of this condition Another important feature of the pathology is that repair once it starts seems to be perfect so that clinically recovery will be complete

Treatment This aims at resting the kidneys as thoroughly as possible until such time as recovery shall have taken place sufficiently for the secretion of urine to be resumed Electrolyte and water balance must be maintained and exogenous protein metabolism reduced to a minimum

No protein is given and as long as there is anuria only sufficient water is allowed to compensate for the fluid lost in the sweat and by breathing This amounts to 1 litre per day Fats and carbohydrates are given so as to provide about 2 000 calories per day The following is the mixture to be prescribed—

Glucose	400 g
Peanut oil	100 g
Acacia q s	to emulsify
Water	to 1 litre

This is the day s ration It is given by means of a continuous drip into the stomach by a fine plastic tube passed through the nose All vomit is collected and returned through the stomach tube This is an important measure for it ensures that the fluid intake is accurate and that electrolytes are not lost by vomiting By this means serious upset of electrolyte balance may be avoided during the period of anuria Once diuresis starts however such imbalance readily occurs and the blood electrolytes will have to be estimated twice daily and the loss made good This does not mean that massive saline or alkaline transfusions can be started The daily fluid requirements are no more than the litre of water in the above prescription with an additional amount equal to the volume of the urine passed the previous day

It has been said that in these types of renal disease recovery when it occurs is apparently complete In a favourable case the anuria is temporary and as soon as sufficient nephrons have been repaired the secretion of urine is resumed Thus if the patient can be kept alive during the period of anuria then the prognosis is good There is every reason therefore for the use of auxiliary methods of excretion

In its most complete form this entails the use of an artificial kidney In this the heparinized blood is led from an artery and is pumped through a long cellophane tube wound round a drum which revolves in a bath of warm Ringer s solution It is then pumped back into the patient s vein

Not only are strict aseptic precautions required but also strict biochemical control is needed for other electrolytes as well as urea, may pass into the bath Prolonged dialysis is not required and the operation is usually completed in four hours Repeated treatments may be required Other methods of reducing the blood urea have been tried these include peritoneal dialysis and the perfusion of isolated loops of small intestine

Chronic Uraemia

Progressive renal disease leading to the damage or destruction of so many nephrons that the kidney is unable to carry out its work efficiently is caused by a variety of disorders There may be congenital abnormalities such as polycystic disease infections such as pyelonephritis inflammations such as glomerulo tubular nephritis In some instances the renal damage is part of a generalized disease as may be the case in malignant hypertension diabetes systemic lupus erythematosus or polyarteritis nodosa

Clinical Picture Three features are responsible for the clinical picture in chronic renal failure whatever may be the underlying cause These are the biochemical upset anaemia and hypertension each may be present to a varying degree in different patients

The patient may or may not give a history of previous renal disease There is tiredness and lack of energy breathlessness and palpitations headaches and failing vision and in some cases convulsions In the late stages drowsiness and coma may occur Oedema is rarely complained of and although frequency and nocturia will be admitted on questioning it is unusual for these symptoms to be volunteered The appetite is poor and repeated vomiting may be the first happening In some cases failure of the left ventricle of the heart or even a cerebral haemorrhage may occur

Uraemic convulsions are occasionally seen They may vary in severity from the minor twitching of isolated muscle groups to typical epileptic seizures with tonic and clonic phases These attacks are due to a sudden increase in the blood pressure and in the tension of the cerebro spinal fluid They are therefore hypersensitive cerebral attacks rather than uraemic convulsions for the disordered biochemistry plays no part in their production

On examination the patient appears ill and grey and he will be wasted and dehydrated In advanced cases there will be stupor and Cheyne Stokes respiration may be present Oedema and ascites are

uncommon The tongue is dry and furred the breath is foul smelling and a urinferous odour may be detectable The peripheral arteries are thickened and tortuous and the blood pressure is almost always raised. Pulsus alternans may be present. The heart is enlarged and there may be an apical gallop rhythm a grave sign Pulmonary oedema may provide further evidence of left ventricular failure Abdominal examination is usually negative but polycystic kidneys or a large hydronephrosis may be felt and gross constipation may produce an easily palpable colon The tendon reflexes may be exaggerated and there may be signs of tetany There may be a severe hypertensive retinopathy with exudates haemorrhages and finally papilloedema

Investigations The urine always contains albumen though the amount may be small it is dilute and as the patient s condition worsens so its specific gravity becomes fixed at about 1·010 Anaemia is always present it is microcytic or normocytic The blood urea is raised but the amount of this does not necessarily reflect the severity of the renal damage If the disease is progressing rapidly then there may be uraemia with only a moderate rise of the blood urea If however the disorder is protracted then the nitrogen retention will occur only very slowly and extremely high levels of blood urea may occur with very little constitutional disturbance The alkali reserve is usually decreased

Important changes may occur in the levels of the electrolytes of the blood In some cases these may dominate the clinical picture to such an extent that the underlying renal failure may not be appreciated Thus in the so-called salt losing nephritis in which sodium is lost the clinical picture may be confused with Addison s disease In the Fanconi syndrome there is an upset in the way in which the kidneys handle phosphate sugar and amino acids

Treatment. This must be symptomatic and palliative rather than curative By the time the patient becomes uraemic the kidneys are almost completely destroyed so that recovery is not to be expected For this reason temporary expedients such as the artificial kidney or dialysation have little place However effective they may be such measures will give only temporary relief and they cannot affect the hypertension or the anaemia Nevertheless something can be done to buttress the failing renal function and to relieve the patient s suffering

Severe cases should be in bed and removal to a hospital where both nursing and laboratory facilities are available may be necessary In the early stages and in mild cases such a move is not necessary and although heavy work is impossible many uraemics can still attend at their office and do very useful work The diet must be low in its protein content about 40 or 50 g if there is oedema the sodium intake will have to be low 500 mg In the absence of anasarca a large fluid intake is essential 4–5 pints may be required each day The aim is to ensure a maximum volume of urine To ensure this the patient may be provided with a large Winchester bottle with graduations in pints painted on it He should be instructed to drink sufficient to fill it to the 5 pint mark every day In advanced cases when anuria supervenes the fluid intake must be reduced and if intravenous alimentation is used care must be taken to see that the circulation is not overloaded. An amount equal to one litre plus the volume of the previous day s urine only should be given An attempt to make good any deficiencies in electrolytes can be made by giving the appropriate substance and the acidosis can be dealt with by using intravenous sodium lactate solution

The anaemia fails to respond to any of the usual haematinics Iron both by mouth and intravenously achieves little The same is true of liver extract cyanocobalamin and folic acid Transfusions of fresh blood will give temporary improvement they must always be given very slowly so as to avoid overloading the circulation

The hypertension is best left untreated unless there is evidence that the patient is standing up badly to it Papilloedema hypertensive cerebral attacks and acute pulmonary oedema are all indications for the use of hypotensive drugs as are signs such as an apical gallop rhythm or pulsus alternans Hexamethonium bromide by injection is the most reliable preparation to use Other preparations such as reserpine and pentolinium are uncertain in their action and may be toxic After a test dose of 25 mg of hexamethonium bromide treatment can be started by giving 50 mg twice daily As tolerance is developed so the dose can be steadily increased

Mecamylamine is a ganglion blocking agent which is effective by mouth in small doses Beginning with 2 5 mg twice a day the dose can be slowly increased until a satisfactory drop in the blood pressure is obtained As with similar drugs constipation may be a troublesome side-effect but more serious toxic manifestations are unusual The use of this drug in cases of nephritis may be dangerous for with a drop in blood pressure renal function may be impaired A careful watch must therefore be kept on the urinary output particularly in the early stages of treatment

Symptomatic measures will include mouth washes to alleviate the foul taste in the mouth Analgesics such as tab codeine co and even pethidine will relieve the headaches Venesection is indicated for severe hypertension if the patient is not too anaemic Lumbar puncture is needed for cerebral

attacks but care should be taken to avoid the for mation of a pressure cone Barbiturates may be used to induce sleep and the restlessness that may occur in advanced cases will often respond to intramus cular injections of paraldehyde Vomiting is always a distressing feature because it is so difficult to control gastric lavage using normal saline may be tried

Renal Involvement in General Disorders

Apart from primary renal disease the kidneys may become involved in certain general diseases Because of their important function this involvement will seriously worsen the prognosis and in many cases it may cause the death of the patient although the underlying malady may not be very advanced Because of their ample blood supply the kidneys are particularly liable to be involved in septicaemia the resulting abscesses are similar to those that occur elsewhere in the body and such disorders need no further description In subacute bacterial endo carditis many infected emboli may lodge in the kidneys giving them a characteristic flea bitten appearance and causing red cells to appear con stantly in the urine It is proposed in this section to deal with the renal changes which may occur in diabetes mellitus in the collagen diseases and in certain types of purpura

Diabetes Mellitus

Patients who have had diabetes for some years usually at least ten may develop albuminuria Apart from this their condition is at first satisfactory except that they always have retinopathy and many micro aneurysms on the capillaries may be seen in the optic fundi Gradually the albuminuria in creases the blood pressure rises and tests will show impairment of renal function with nitrogen reten tion As the disease progresses so the amount of insulin the patient requires may drop and in the terminal stages a previously severe diabetic may require no insulin at all

At autopsy particular changes first described by Kimmelstiel and Wilson whose names have been given to the syndrome are found The glomeruli are especially affected and there is a deposit of amorphous material as well as fibrosis actually within the network of the glomerular tuft—so-called intracapillary glomerular fibrosis The constant find ing of damaged capillaries in the optic fundi sug gests that a similar pathology may occur in the kidneys There is no particular treatment of this diabetic nephrosclerosis

The Collagen Diseases

In both polyarteritis nodosa and systemic lupus erythematosus the kidneys may be involved with characteristic pathological changes In both dis orders the clinical picture may be that of the nephrotic syndrome or of chronic renal failure In addition there will usually be evidence of the wide spread underlying disease In both diseases the blood sedimentation rate is greatly raised and in systemic lupus erythematosus the L E-cell phe nomenon may be present. In polyarteritis nodosa the active disease may be over and the renal impairment comes as a result of the scarring of the kidneys as the vascular lesions heal

Purpura—the Schönlein Henoch Syndrome

The occurrence in children of purpura with joint pains and swellings led to the description of rheu matic purpura or Schonlein s disease Similarly the combination of purpura and bleeding from the in testinal tract was known as abdominal purpura or Henoch s disease In both disorders the occurrence of haematuria has been frequently recorded and recent studies of large series of patients show that the two diseases are not clear-cut and although in a few instances the systemic manifestations may be confined to either the joints or the intestines in most cases there is purpura joint pains intestinal haemorrhage and haematuria The latter feature is due to a nephritis in which histologically a necro tizing arteriolitis is a prominent feature The prog nosis in this form of purpura is bad progressive renal disease frequently occurring In the course of this the nephrotic syndrome or chronic renal failure may occur and in each instance the persistence of haematuria is a characteristic feature

The Kidney and Hypertension

The almost constant finding of hypertension in chronic renal disease has led to the conclusion that the damaged kidneys in some way cause the hyper tension This conception was in fact suggested by Richard Bright who noted the association of con traction of the kidneys and hypertrophy of the

heart. At first it was considered that the kidneys were always responsible for hypertension even when there was no demonstrable renal disease In time this concept was abandoned but not before it had been demonstrated that an enzyme renin derived from the kidney could under certain circumstances cause hypertension

Direct, as opposed to circumstantial evidence of the relation between the kidneys and hypertension was a long time coming It was not until 1934 that Goldblatt and his colleagues in America showed that the constriction of both renal arteries in dogs was followed by sustained hypertension Later it was shown that the clamping of one renal artery was effective As a result of this work unilateral renal disease as a cause of hypertension became a popular theory and many kidneys must have been removed by enthusiastic surgeons as a result of injudicious reports on intravenous pyelograms With the passage of time however it was realized that it was extremely rare to find a hypertensive patient with one damaged kidney and it was even more rare for the removal of the kidney to be followed by subsidence of the raised blood pressure

Nevertheless successful cases do occur and it is among young individuals or in older subjects who are definitely known to have had hypertension for a short while that examples should be sought. Every established hypertensive patient below the age of forty should have a full urological examination and the younger they are the more important this is Ideally the unaffected kidney should be normal but successes have been recorded where relief of the hypertension has been followed by an improvement in the function of a slightly impaired kidney In the evaluation of these cases as in the elucidation of all obscure renal disease needle biopsy of the kidney may be most helpful

If it is natural to assume that chronic Bright s disease causes hypertension the frequent association of the two disorders also raises the possibility that prolonged hypertension may cause renal disease This too has been shown by experiment on animals to be so Evidence from human pathology is shown by the frequency with which renal sclerosis is found at autopsy in elderly people known to have had a raised blood pressure for many years

Malignant Hypertension

A patient with hypertension of any sort may suffer from a sudden deterioration of his condition The diastolic pressure rises alarmingly albuminuria if not already present becomes marked and retinopathy in which papilloedema is a prominent feature occurs Death ensues within a short while of the development of the condition either from renal failure cardiac failure or cerebral haemorrhage or sometimes from a combination of all three This malignant termination of a previously-existing hypertensive state not only carries with it a special prognosis but also has a particular pathology There is a necrotizing arteriolitis which is found in organs other than the kidney but which particularly affects the afferent glomerular arterioles

It must be emphasized that malignant hypertension is not a term which is loosely applied to any condition in which the blood pressure is extremely high particularly if the patient is young It should be applied only to hypertensives who have albuminuria and papilloedema As the condition usually develops on a previous long standing hypertension or renal disease it is seen in old rather than young subjects

The Kidney in Pregnancy

A urinary infection is the commonest disorder of the renal tract in pregnancy Not only do the ureters become hypertrophied so that their course becomes tortuous but the enlarging uterus can press upon them as they cross the pelvic brim There is thus considerable interference to the flow of urine and infection by *E coli* from the neighbouring bowel can readily occur When this happens the clinical picture is similar to that produced by the disease in non pregnant patients Vigorous treatment with the appropriate sulphonamide or antibiotic is required and throughout pregnancy the patient should be instructed to drink large quantities every day

Less frequent but almost more important is the question of hypertension and renal failure in pregnancy There are three possibilities A known pre existing benign hypertension or nephritis may be aggravated by the pregnancy A latent or previously unrecognized hypertension or nephritis may be unmasked by the pregnancy Thirdly damage may be done to previously healthy kidneys by the toxaemic condition of pre eclampsia this damage may result in a permanently raised blood pressure

In each instance there will be hypertension oedema and albuminuria In the absence of any history of previous renal disease it may be impossible to make an exact diagnosis though this will not necessarily interfere with the management of the

case Obstetricians *adopt the view* that before the 20th week the condition is due to a pre existing hypertension or renal disease while after that time the condition is one of pre eclampsia

In treatment the all important factor is complete *rest for the patient* This is the *only measure* which has been shown to reduce the chances of permanent damage to the mother and to give some hope of there being a live baby but stillbirth is almost inevitable Hypotensive drugs are not recommended for *there is some evidence* that they *can cause the* death of the foetus

The physician will be consulted by his female patients who are known to be hypertensives or chronic nephritics as to the advisability of pregnancy *He may* be asked whether a pregnancy in such a patient should be allowed to continue or should be *terminated* No hard and fast rule can be given and each case must be separately considered The chances of such patients having a live baby if their renal disease *is* of any severity *are* slender The chances that their condition will be worsened by the *pregnancy* are high On the face of it *there*fore termination would seem to be the best advice Nevertheless some of the patients will have live babies without doing themselves any great additional harm Others may get to perhaps the sixth month *before* they *miscarry* Such an *experience* may go a long way towards satisfying the patient s *longing for a* child of her own a *longing* that may later be further satisfied by the adoption of a baby

If however pregnancy is allowed the position must be made clear to both partners The most careful supervision must be *exercised* and immediate *admission* to hospital arranged at the *first sign of* trouble

Low Sodium Diet

No Salt to be Used in Cooking No Salt at Table

Bread Not more than three whole slices a day Oat cakes made without salt are recommended

Milk should be diluted with half its bulk of water

Salt free margarine should be used *Lard or dripping* should be used in cooking wherever possible

Eggs are best fried or poached

The simple meats—beef mutton lamb pork and rabbit—are best *All* gravy salted and preserved meats meat extracts like Marmite Bovril or Oxo are forbidden Bacon and ham are *prohibited*

Steamed white fish is allowed in small helpings also *fish cakes made with rice without salt and deep fried* in olive oil Smoked fish (kippers haddock) tinned *fish and fish paste are prohibited*

Rice semolina sago and macaroni puddings *(made with diluted milk) are allowed*

Fresh fruit stewed fruit and tinned fruit are allowed

Any vegetables (cooked without salt) *except* beetroot, carrots celery spinach *No* tinned vegetables

Tea coffee lemonade or water *No* milk drink such as Ovaltine Horlicks Bournvita

No cheese

No foods made with baking powder (cakes *suet puddings* Yorkshire pudding)

CHAPTER 19

Diseases of Blood

C C THOMAS

General Considerations

THE disorders known as blood diseases are those affecting the cellular elements of the blood These cells are formed in the red bone marrow and perform their functions in the general circulation The physiological organ of blood stream and bone marrow considered as a whole has been called the erythron In foetal life blood cells are first formed in the yolk sac and later in the liver spleen and thymus finally they are produced by the marrow which is the sole organ of haemopoiesis at birth During infancy active red marrow is present in all bones That in the limb bones is gradually replaced by fatty yellow marrow during childhood until by adult life red marrow is confined to the skull the bones of the trunk and small areas at the upper ends of the femur and humerus

When it is desired to study blood formation the tibia is a suitable site for marrow puncture in infants but in adults the usual sites are the sternum iliac crest and the spinous processes of the vertebrae As the marrow is semifluid in life fragments can be aspirated by suction through a special needle from which films are made and stained in the same way as films of peripheral blood Such preparations are always contaminated with peripheral blood but this does not affect the usefulness of the method In some cases blood can be separated from marrow fragments and sections cut When the marrow is unduly dense as when it has been replaced by fibrous tissue marrow puncture may be unsuccessful but a biopsy may then be taken of the marrow either by removing a small piece of rib or trephining the sternum

There are two main theories as to the continued production of the cellular elements of the blood According to the monophyletic theory a single totipotential cell of the marrow the haemocytoblast is capable of differentiation into all the mature cellular types According to the polyphyletic theory the precursors of the mature cells are from the start differentiated From a practical standpoint however the cells usually found in films of bone marrow can be classified as already belonging either to the erythrocytic or to the leucocytic series

All nucleated cells which are precursors of erythrocytes are collectively known as *erythroblasts* The most primitive of these is the *proerythroblast* which divides and produces smaller nucleated cells known as *normoblasts* These are usually classified into different types on the basis of their maturity and are most simply referred to as early intermediate and late normoblasts. These cells all take part in normal erythropoiesis In certain disorders such as pernicious anaemia normoblasts cannot be produced owing to the lack of essential substances instead the proerythroblasts give rise to abnormal nucleated cells the *megaloblasts* These cells are also subdivided into early intermediate and late forms but are larger and have a more pronounced reticular arrangement of chromatin in their nuclei and show precocious haemoglobinization as compared with the corresponding normoblasts Cells of megaloblast type may be found in normal foetal life when for the first few months all erythrocytes are nucleated After birth megaloblasts are abnormal and their presence indicates a condition known as megaloblastic anaemia in which the circulating erythrocytes are typically larger than normal

In leucopoiesis the most primitive cells usually observed in the marrow are *myeloblasts lymphoblasts* and *monoblasts* These cells are larger than the mature cells into which they develop and may be recognized by the presence of nucleoli which are later lost Different types of blast cell can be distinguished from one another only with difficulty Myeloblasts give rise to polymorphonuclear neutrophil leucocytes and eosinophil and basophil leucocytes through intermediate cells called *myelocytes* These myelocytes have specific neutrophilic eosinophilic or basophilic granules but their nuclei although devoid of nucleoli are not yet segmented Neutrophil myelocytes are often further subdivided according to their maturity into premyelocytes myelocytes and metamyelocytes Lymphoblasts and

monoblasts give rise to fully formed lymphocytes and monocytes

Extremely large cells with lobed nuclei the *megakaryocytes* are also present in the marrow These give rise to *thrombocytes* usually known as *platelets* by budding off from their cytoplasm

Normal Values The volume of the circulating blood including both cells and plasma ranges from 4 to 8 litres (*78–97 ml/kg of body weight*) The erythrocyte count ranges in adults from 4 2 million to 6 4 million/mm³ with means of 5 5 million for males and 4 8 million for females Haemoglobin values for normal adult males lie between 14 and 17 g/100 ml with a mean of 15 6 g/100 ml and for females between 12 and 15 5 g/100 ml with a mean of 13 7 g/100 ml Infants at birth have over 15 g/100 ml which falls to about 11 g/100 ml in a few weeks In childhood both sexes have values similar to those of women It has long been customary for haemoglobin values to be expressed as a percentage and it has been decided by international agreement *that 100 per cent is equal to 14 6 g/100 ml*

The life span of erythrocytes in the circulation is about 120 days When they first appear in the peripheral blood erythrocytes can be shown by supravital staining with cresyl blue to have a network of primitive cytoplasmic remnants These young cells are called *reticulocytes* they normally number up to 2 per cent of the total erythrocytes but they may be greatly increased when there is an excessive outpouring of cells from the marrow Erythroblasts are not normally found in the peripheral blood

The normal leucocyte count in adults lies between 4 000 and 11 000/mm³ The neutrophil polymorphonuclears range from about *2 000–7 500* lymphocytes from 1 000–3 500 monocytes 0–800 eosinophils 0–400 and basophils 0–200 The cells of the last three varieties are too scanty to make accurate enumeration possible when the usual method of doing a differential leucocyte count is employed Accurate eosinophil counts may be made by direct enumeration in a counting chamber using special diluting fluid The finding of myelocytes and blast cells in the peripheral blood is abnormal *In* severe infections there may be a few myelocytes in the peripheral blood and the neutrophils are of a primitive form with fewer lobes to their nuclei the so called *shift to the left* At birth there is a slight neutrophil leucocytosis which disappears in a few days Thereafter until the age of 12 there is a slight lymphocytosis so that the numbers of neutrophils and lymphocytes are approximately equal

The platelets normally number *150 000 to* 350 000/mm³ Megakaryocytes are found only in the peripheral blood in pathological states and then very rarely

Disorders of the blood principally manifest themselves by the production of anaemia in which the total number of circulating erythrocytes and haemoglobin is reduced This is usually detected by the erythrocyte count and haemoglobin estimation However these methods measure concentrations and do not distinguish between anaemia and hydraemia in which the plasma volume is increased and the mass of circulating cells unaltered To distinguish the two conditions with certainty the blood volume must be determined this is technically difficult and a diagnosis can nearly always be established by *other means Some anaemias* such as those occurring in nephritis and pregnancy are possibly due in part to hydraemia

There are other methods in addition to the erythrocyte count and haemoglobin estimation of indicating both the presence of anaemia and its type By centrifuging samples of blood in calibrated tubes of uniform bore known as haematocrit tubes the *packed cell volume* or haematocrit can be measured This is simply the ratio of the volume occupied by the cells to the total volume and is normally 45 per cent By equating erythrocyte count and haemoglobin the amount of haemoglobin in each individual cell can be *determined* In practice it is simpler to calculate the colour index which is the ratio of the percentages of normal of the erythrocyte count and haemoglobin For this purpose it is arbitrarily assumed that the erythrocyte count is normally 5 million/mm³ and the haemoglobin 100 per cent Colour index is then

$$\frac{\text{observed haemoglobin \%}}{\text{erythrocyte count in millions} \times 20}$$

A colour index of more than 1 indicates that each cell contains more than the average amount of haemoglobin and a colour index of less than 1 indicates the reverse By equating packed cell volume with the erythrocyte count the average volume of the individual cell can be measured this is known as the *mean corpuscular volume* (MCV) If the haemoglobin is equated with the packed cell *volume the concentration of haemoglobin* in the erythrocyte mass can be determined this is known as the *mean corpuscular haemoglobin concentration* (MCHC) The *mean corpuscular diameter* can be determined directly by measuring the diameters of projected images of a number of erythrocytes at a given magnification and constructing a frequency distribution curve called a Price Jones curve after its originator but in practice this is too time-con*suming The alternative method of indirect measurement depends on the optical phenomenon of diffrac*tion and is too inaccurate to be used much to day Cell diameters may be roughly estimated as normal

or *normocytic* large or *macrocytic* and small or *microcytic* by microscopic examination of a stained film At the same time the presence or absence of *anisocytosis* indicative of cells of widely-divergent diameter and *poikilocytosis* or cells of unusual shape may be noted If the cells stain faintly with the eosin component of the normal Romanovsky stains they are called *hypochromic* indicative of a low MCHC Reticulocytes under these conditions may stain rather more purplish than pink and the film is said to show *polychromasia* when this is pronounced Some reticulocytes contain bluish black dots called *punctate basophilia* when stained in this manner This is particularly characteristic of lead poisoning but may occur in any severe anaemia The presence of erythroblasts and changes in the leucocyte and platelet counts may provide additional information

By the use of the mean corpuscular volume anaemias may be divided into three main classes normocytic microcytic and macrocytic depending on whether the cells are on the average of normal size small or large The colour index which is normally 1 is usually greater than 1 in macrocytic anaemias and less than 1 in microcytic anaemias However if a macrocytic anaemia is accompanied by deficient haemoglobin production the colour index may be 1 or even less although the MCV is increased The use of the colour index should therefore be abandoned in favour of the MCV and MCHC Of these two determinations the MCHC is by far the most useful When reduced below its normal range of 32–38 per cent it indicates lack of haemoglobin production and in general the need for iron therapy Changes in the MCV cannot be so safely correlated with therapeutic needs Macrocytic anaemias are by no means invariably indicative of megaloblastic erythropoiesis and therefore therapy should not be based solely on the finding of an increased MCV

The MCHC can be calculated very accurately as it depends on the haemoglobin and packed-cell volume both of which can be determined to within ± 2 per cent after the blood has been collected from the patient The MCV on the other hand depends on the erythrocyte count which is most inaccurate unless great care is taken In addition to errors in filling the counting chamber the standard error is the square root of the number of cells counted If for example 400 cells are counted 19 out of 20 repeat counts will lie between 360 and 440 If these 400 cells represent a count of 4 million/mm³ repeat results will lie between 3 6 million and 4 4 million/mm³ It is thus clear that in order to obtain erythrocyte counts of an accuracy corresponding to those of haemoglobin and packed-cell volume determinations a great many cells must be most laboriously counted To facilitate this electronic erythrocyte counters are being developed but until they are available erythrocyte counts should be reserved for special cases

In the vast majority of instances the presence or absence of anaemia and an indication as to its type may be obtained from the haemoglobin determination MCHC and microscopic examination of the stained film In addition leucocyte platelet and reticulocyte counts or marrow puncture may be needed in selected cases The error of collecting blood samples physiological fluctuations and technical error all added together are such that a change in the patient s degree of anaemia cannot be assumed to be present unless a repeat determination differs by about 1 5 g/100 ml haemoglobin or 10 per cent on the percentage scale

Anaemia

Pathology The general effect of anaemia on the organs of the body is deficient oxygenation When the anaemia is acute following a sudden haemorrhage the blood volume including the plasma volume is greatly reduced the cardiac output falls and death may result from cerebral anoxia In chronic anaemias long-continued oxygen lack may produce fatty degeneration of organs which in the heart may lead to myocardial failure Plasma volume is approximately normal and the circulation is adapted for a small erythrocyte volume A transfusion therefore if at all rapid may throw a strain on the damaged myocardium and lead to death from pulmonary oedema If given in chronic anaemias transfusions should consist of small slow infusions of packed cells and the greater the degree of anaemia and the age of the patient the greater the caution required

Clinical Picture *Following an acute haemorrhage* there are usually no symptoms unless the loss exceeds 500 ml A loss of 700 ml produces slight symptoms greater losses more severe symptoms and a sudden removal of 1 500–2 000 ml may prove fatal Larger losses may be withstood if spread over 24 hr or more There is a profound fall in blood pressure and reduced cardiac output The skin is cold pale and sweating the pulse rate is increased and the respirations sighing and rapid There may be giddiness faintness and occasionally loss of consciousness Visual disturbances and even blindness may occur

Prominent symptoms of chronic anaemias are

tiredness and listlessness though they also occur frequently in people who are not anaemic Dyspnoea on exertion is common headaches and fainting may occur Vague ill health associated with pallor is very suggestive but pallor of itself may be misleading The skin often shows considerable pallor in the absence of anaemia and the tint of the mucous membranes is more reliable The conjunctivae are often examined but local conditions may make them unduly pink and examination of the palate is more satisfactory Nevertheless many people have quite marked degrees of anaemia without its being clinically apparent and others seem anaemic when they are not *Chronic anaemia* may give rise to systolic murmurs (known as haemic murmurs) due to cardiac dilatation Palpitation and oedema of the ankles are common and even anginal pain and congestive cardiac failure may occur without other gross cardiac disease When the anaemia is severe there may be fever of up to 100°F and paraesthesiae of the extremities Apart from pallor and haemic murmurs physical examination may in certain types of anaemia reveal jaundice splenomegaly lymphadenopathy or purpura

Causes These may be summarized as follows—

1 Increased removal of erythrocytes from the circulation

(a) Haemorrhage

(b) Haemolysis

2 Impairment of blood formation (Dyshaemopoietic anaemias)

(a) Deficiencies of substances necessary for normal blood formation (Haematinic principle Iron Protein Hormones and Vitamins)

(b) Destruction of blood producing tissue (Aplasia and Hypoplasia)

(c) Displacement of blood producing cells (Leuco-erythroblastic anaemias)

(d) *Depression of Erythropoiesis* (*Sepsis* Nitrogen retention Malignant disease etc)

Principles of Treatment The keystone of successful treatment is accurate initial diagnosis It may seem self evident that iron will cure only iron deficiency states but it is frequently given for all kinds of anaemia including that due to infection If there is no need for iron but it is given orally it is merely not absorbed if given parenterally it is stored in excessive amounts A similar excessive storage follows blood transfusion but this has the merit of causing an initial rise of haemoglobin Vitamin B_{1} and folic acid are only of benefit in megaloblastic anaemias Pharmaceutical houses have produced many preparations containing mixtures of haematinics presumably in the hope of treating anaemia without the need to examine the blood beforehand To use them is most unwise In the first place persons are treated for anaemia who are not anaemic at all secondly the different constituents of such preparations are often in inadequate individual dosage and lead to slower recovery and thirdly in unsuspected cases of pernicious anaemia the clinical picture is obscured and this leads to an increased likelihood of the development of subacute combined degeneration of the spinal cord Transfusion for chronic anaemia should be used only in cases refractory to haematinics or in need of immediate surgery Its effect is purely temporary and its use accompanied by risks from circulatory overloading and transfusion reactions There are no general measures applicable to the treatment of anaemia bed rest is of no benefit of itself but is indicated if asthenia is marked Grossly deficient diet needs correcting but the use of supplements is valueless

Iron-deficiency Anaemia

The commonest type of anaemia is that due to lack of iron It occurs about a hundred times as commonly as pernicious anaemia

Aetiology The average life of an erythrocyte is 120 days as a result the normal daily destruction yields 26 mg of iron In men about 1 2 mg of this is excreted in approximately equal amounts in bile and urine the rest is conserved and used again Women lose slightly less in these ways but when menstruating also lose 10–40 mg at each period making in all an average daily loss of about 2 mg In addition the body contains iron reserves sufficient to replace about one quarter of the circulating haemoglobin The iron content of a satisfactory diet is about 20 mg daily but only about 4 mg are in a form available for absorption Many people subsist on a diet considerably poorer in iron There is no entirely satisfactory method of determining the availability of iron but inorganic iron is more readily absorbed than organic and ferrous than ferric In general iron is absorbed only when the iron reserves are depleted otherwise it is excreted unchanged in the faeces Haemochromatosis is probably caused by the uncontrolled absorption of iron due to a breakdown in this mechanism Iron absorption seems to be assisted by an acid reaction and

occurs in the stomach and upper part of the small intestine

Iron deficiency anaemias are commonly caused by chronic haemorrhage typically uterine Many haemorrhagic lesions of the intestinal tract also reveal themselves by anaemia When it is realized that a loss of 10 ml of blood is equivalent to a loss of 5 mg of iron this is not surprising In a few subjects anaemia due to small continued intestinal haemorrhage may be caused by the regular ingestion of salicylates Deficient amounts of iron in the diet are common particularly where there is an extra demand as in premature infants growing children and in pregnancy during the course of which about an extra 500 mg of iron is required for the foetus Failure to absorb iron is the cause of the majority of post gastrectomy anaemias and of the anaemias accompanying steatorrhoea and achlorhydria This type of anaemia is commonest in women before the menopause If there is no haemorrhage or dietary deficiency to account for it it is called idiopathic hypochromic anaemia Although women are affected about twenty times as commonly as men it is not so rare in males as originally thought It has been found to affect a small proportion of National Service men in whom no obvious nutritional defect occult haemorrhage or failure of absorption is discovered

Clinical Picture In addition to the usual symptoms of chronic anaemia dyspepsia and glossitis may occur Some 15 per cent of women with the idiopathic variety of the disorder have a peculiar form of dysphagia known as the Plummer Vinson syndrome This takes the form of difficulty in swallowing solids referred to the level of the larynx Definite webs in the oesophagus may be formed which can be seen with an oesophagoscope or in a barium swallow and post-cricoid carcinoma occasionally develops later The nails may become spoon shaped thin and brittle a deformity known as koilonychia The spleen is occasionally just palpable but in the vast majority of cases it is of normal size Paraesthesiae of the extremities are present in a few instances

Blood Picture The principal feature is a hypochromic anaemia due to failure of haemoglobin synthesis The erythrocytes are only slightly reduced in number the haemoglobin is proportionately much lower the packed-cell volume (PCV) is intermediate As a result the colour index is less than unity and the mean cell volume (MCV) and mean corpuscular haemoglobin concentration (MCHC) are low The leucocytes are normal or slightly reduced in number and the platelets are normal Reticulocytes are typically less than 10 per cent and the erythrocytes in the stained film are hypochromic and microcytic with some anisocytosis and poikilocytosis The serum bilirubin is low the pallor of the plasma often being a conspicuous laboratory feature Achlorhydria is common but of no diagnostic significance The serum iron is low but the diagnosis can be made without its aid The bone marrow shows normoblastic hyperplasia but marrow puncture need not be done as the peripheral blood picture and particularly the MCHC are sufficient for haematological diagnosis

Differential Diagnosis The blood picture is so distinctive that there is usually little difficulty in making the diagnosis A few cases of pernicious anaemia may have concomitant iron deficiency This dual pathological state would be suspected if there is a high MCV or other evidence of macrocytosis accompanying a low MCHC Marrow puncture will then elucidate the problem Thalassaemia has a low MCHC without iron deficiency but is otherwise easily distinguished and is very rare in Britain Finally it is important to remember that the diagnosis iron deficiency anaemia is not always sufficient as it is often secondary to occult bleeding especially from malignant disease of the bowel

Course Untreated the disease continues indefinitely unless the patient s iron balance is improved as may happen at the menopause Treated cases tend to relapse when therapy is discontinued but no satisfactory criteria exist for predicting future relapse This is probably because it is difficult in many cases to assess whether the cause is nutritional haemorrhagic defective absorption or a combination of all factors each in itself of minor degree

Treatment This consists of adequate iron therapy preferably by mouth If a third of the proper dose is given the haemoglobin does not take three times as long to rise but usually remains stationary Tab ferrous sulphate co B P C 0 4 g (6 gr) t d s is the cheapest preparation and usually extremely effective Its disadvantages are that some people particularly pregnant women are resistant to it and that it more often gives rise to gastro intestinal upsets than other oral preparations Ferrous gluconate 650 mg (10 gr) t d s or ferrous succinate 150 mg (2 5 gr) t d s are considerably more expensive but in some cases are better tolerated and more effective Chelated iron (Sytron) in a dose of 8 ml (two teaspoonfuls) t d s for adults is palatable and has few side effects For children in smaller proportional doses according to weight it is particularly satisfactory If treatment is successful the haemoglobin rises by about 0 2 g/100 ml per day Occasionally the rise is even faster Because of the inherent error of haemoglobin determinations particularly that involved in collecting blood samples it may not be

possible to demonstrate whether the response is satisfactory until therapy has continued for a fortnight A reticulocyte increase can rarely be used to demonstrate that treatment is successful because it depends on an initial low erythrocyte count which is unusual If oral therapy is unsuccessful as when there is defective absorption or if rapid recovery is imperative parenteral iron should be used Two types of preparation are available sacharrated oxide of iron Ferrivenin" or Iviron for intravenous use and a dextran iron complex Imferon for intramuscular use The intravenous preparations contain 100 mg of iron in 5 ml They often cause symptoms which include flushing syncope headache substernal pain tachycardia and occasionally profound collapse These can be minimized by starting with a dose of 20 mg and increasing it slowly The intramuscular preparation 'Imferon causes pain and staining at the site of injection and it has been found experimentally to cause sarcomata in rats Theoretically all the iron given parenterally is utilized and it is possible to calculate from the initial haemoglobin level how much is needed to be given to raise it to normal. Up to 5 ml of 'Imferon (250 mg iron) may be given daily to elderly people each dose should raise the haemoglobin of an average sized person by 1 48 g per cent This may not happen to its full extent during th course itself and the haemoglobin may continue to rise after it is finished If parenteral iron is given to the patient who is not iron deficient it is stored in the reticuloendothelial system as is the iron derived from transfusions of whole blood The amounts of iron so laid down may rival those of haemochromatosis but the cellular damage of that disease does not occur Nevertheless it is clear that it is more physiological to give iron by mouth provided it is absorbed

Megaloblastic Anaemias

Pernicious Anaemia

This disease first described by Addison is so named because it always ended fatally until the discovery of liver therapy by Minot and Murphy in 1926 It is a disease of great importance as once diagnosed treatment must be continued for life and the consequences of inadequate treatment may be disastrous It is not particularly common each general practitioner may see on the average a new case every two to five years

Aetiology Castle s extrinsic factor now known to be vitamin B_{12} or cyanocobalamin must be absorbed from the food to enable normal haemopoiesis to occur This absorption is made possible by the secretion of intrinsic factor by the stomach and in its absence pernicious anaemia develops The loss of the power to secrete intrinsic factor is essentially part of the process of ageing and consequently the condition is rare before the age of forty When it is found in a young adult it is usually accompanied by premature greying of the hair About 8 per cent of cases show a familial incidence The sexes are equally affected but an unexpectedly large number of cases of pernicious anaemia are of blood group A

Pathology The organs are pale and fatty as a result of the anaemia The bone marrow is hyperplastic red marrow replacing the normal yellow of the long bones The gastric mucosa is atrophic Evidence of increased blood destruction is suggested by slight jaundice and the presence of haemosiderin in the reticuloendothelial system The spinal cord may show demyelination whi h in extreme cases involves the whole of the circumference of the cord apart from a narrow ring surrounding the grey matter

Clinical Picture The onset is insidious In addition to the symptoms of chronic anaemia a common complaint is soreness of the tongue which is seen to be smooth and atrophic This is even more characteristic of pernicious anaemia than of iron deficiency anaemia The skin may be slightly lemon yellow Petechial haemorrhages are rare Weight loss is unusual Due to the gastric dysfunction dyspepsia may be prominent In a few cases subacute combined degeneration of the cord (*see* p 466) is present from the outset The earliest symptom of this may be paraesthesia of the extremities, though these may occur in any anaemia Mental symptoms such as loss of concentration and confusion may also occur

Blood Picture When first seen the anaemia is often profound persons with haemoglobins of 5 g/100 ml being occasionally ambulant Typically the colour index is high the MCV high and the MCHC normal unless there is an associated iron deficiency The leucocytes are reduced in number and the polymorphs show hypersegmentation having up to 7 lobes in their nuclei The platelet count is low There is usually an increase in indirect bilirubin In films the erythrocytes are macrocytic and show marked anisocytosis and poikilocytosis but have a normal haemoglobin content The reticulocyte count is usually under 5 per cent In severe cases the typical large nucleated erythroblasts with precocious haemoglobinization and reticular nuclei the megaloblasts may be found Marrow puncture reveals megaloblastic erythropoiesis peculiar large

distorted metamyelocytes (giant stab cells) and few megakaryocytes Gastric analysis shows histamine resistant achlorhydria because the stomach loses the power to secrete hydrochloric acid before it fails to produce intrinsic factor

Diagnosis. As treatment must be continued for the remainder of the patient s life the diagnosis of pernicious anaemia should never be made lightly An essential criterion is the demonstration of megaloblasts in peripheral blood or marrow The presence of free HCl in a gastric analysis virtually excludes the disease lack of intrinsic factor in the presence of free HCl has been confirmed in a very few cases by feeding their gastric juice to known untreated cases of pernicious anaemia Microbiological assay has shown that such cases in common with ordinary cases of pernicious anaemia have a low level of serum vitamin B_{12} and show deficient absorption of an oral test dose of radioactive vitamin B_{12} By contrast the mere finding of histamine resistant achlorhydria is of little help in reaching the diagnosis as it is fairly common in the age group concerned Gastric biopsy through a gastroscope shows a more or less specific histological type of atrophy but is not required in normal practice Diagnosis may be finally clinched by demonstrating a reticulocytosis maximal five days after parenteral vitamin B_1

Course and Treatment Untreated partial remissions may occur spontaneously once or twice but the disease is inevitably fatal Subacute combined degeneration of the cord may develop if it has not accompanied or preceded the anaemia but only if treatment is inadequate Adequately treated cases have a somewhat increased liability to develop carcinoma of the stomach but it is rare for cases of carcinoma of the stomach to present with a megaloblastic anaemia due to the direct destruction of the intrinsic factor secreting portion If treatment is stopped after being adequate initially relapse may become manifest in a few months or may be delayed for up to 4 years

Before the discovery of vitamin B_{12} it was thought that extrinsic factor combined with intrinsic factor to form a haematinic principle which was stored in the liver extracts of which cured the anaemia It is now apparent that parenteral extracts are effective by virtue of their content of vitamin B_{12} The reason why liver should be effective by mouth is not so clear but probably it is related to the large amount eaten Vitamin B_{12} in doses of 3 000 μg may also be effective orally The potency of liver extracts can be assessed only by comparing their effects on untreated cases or by assaying their vitamin B_{12} content microbiologically Pernicious anaemia can be adequately treated in every way by the oral administration of extracts of hog s stomach which contain intrinsic factor Pteroylglutamic acid (folic acid) will induce an haemotological remission in pernicious anaemia when given orally but on the other hand it seems to accelerate the appearance of neurological complications Folic acid probably acts at a different stage from vitamin B_{12} in the maturation of erythroblasts and is effective by mass action in correcting the haemotological but not the neurological manifestations of pernicious anaemia

Parenteral vitamin B_{12} is now the established remedy for pernicious anaemia There is probably no place for liver extracts because they may cause sensitization reactions and because the factors other than vitamin B_{12} which they contain are of no proven value A satisfactory clinical response has been obtained with doses of the order of 12 5 μg vitamin B_{12} but it is wiser to give 200 μg twice weekly until the blood picture is normal bearing in mind that there are normally body stores of about 2 000 μg The same dose should then be given fortnightly or monthly for maintenance Vitamin B_{12} will arrest the nervous complications but little improvement in established cases is to be expected Successful treatment with vitamin B_{12} results in the haemoglobin rising by 0 2 g/100 ml or more per day The reticulocyte response to be expected on the fifth day depends on the initial erythrocyte count it is 35 per cent if the initial count is one million and 8 per cent if it is 2 5 million

All treated cases should have their haemoglobin levels determined and a film examined for erythrocyte abnormalities every four to six months as cord symptoms may develop when the patient feels well although his blood shows early relapse Some cases have an associated iron deficiency which may not manifest itself until treatment has begun as the need for iron is then greater For this reason the MCHC should be estimated at intervals during treatment A patient rarely relapses in spite of increasing the maintenance dose of vitamin B_{12} and in the absence of iron deficiency In such a case folic acid 5 mg t d s may be given orally *provided parenteral vitamin B_{12} is continued simultaneously* If patients are desperately anaemic when first seen blood transfusion must be considered It should be remembered that the anaemia has probably been just as profound for some time and that vitamin B_{12} will produce a definite improvement in a week On the other hand blood transfusion increases the blood volume and may kill the patient who probably has a fatty myocardium However if the risk is understood it is probably relatively safe to give up to one pint of packed cells at one time by a slow drip

Other Megaloblastic Anaemias

These are all less common in Britain than classical pernicious anaemia and they carry little or no risk of serious neurological complications They are presumed to be due to the lack of substances necessary for the *proper maturation of erythroblasts* as all show megaloblasts in the bone marrow Some respond to vitamin B_{12} and some to folic acid

The defect responsible in each particular case may be predicted by estimating the following the level of serum vitamin B_{12} the absorption of radioactive vitamin B_{12} when given orally and the excretion of folic acid after a test dose In practice, however sufficient information is gained from a therapeutic trial assessed by reticulocyte counts Defective absorption is the probable explanation of the megaloblastic anaemia of tropical sprue and idiopathic steatorrhoea of adults children with coeliac disease usually have an iron deficiency anaemia The blood picture may be very similar to that of pernicious anaemia but vitamin B_1 has little or no effect there being a feeble or absent reticulocyte response 5 days after it is given Folic acid on the other hand is dramatically effective Defective fat absorption and other stigmata of steatorrhoea are often present though diarrhoea and other abdominal symptoms may be absent or slight There may or may not be histamine resistant achlorhydria

Megaloblastic anaemia indistinguishable from classical pernicious anaemia may occur after total or extensive partial gastrectomy It is due to loss of intrinsic factor and responds to vitamin B_{12} It is far less common than post gastrectomy iron deficiency anaemia Other intestinal lesions may *cause folic acid deficient* megaloblastic anaemia by mechanical interference with absorption and in animals it has been produced experimentally by the formation of blind loops

The so called pernicious anaemia of pregnancy of western countries is a megaloblastic anaemia responding to folic acid but not usually to vitamin B_{12} The blood picture is not so characteristically macrocytic as the classical disease so that marrow puncture is advisable in all anaemias of pregnancy that are not obviously iron deficient The disease is more common in multiparae Free HCl is usually present in the stomach Although the anaemia may recur in subsequent pregnancies it does not relapse after parturition and permanent treatment is not required

Nutritional megaloblastic anaemias are very common in the tropics but differ significantly from each other owing to differing dietetic habits in various countries Some are cured by Marmite or vitamin B_{12} orally In Finland and Russia a proportion of those infestated with the tapeworm *Diphyllobothrium latum* develop megaloblastic anaemia indistinguishable from pernicious anaemia except that expulsion of the worm produces a reticulocytosis and clinical cure The worm is thought to cause anaemia by itself absorbing vitamin B_1 and so depriving the host. *Megaloblastic* anaemia develops occasionally in patients having phenytoin sodium therapy for epilepsy It responds well to folic acid and variably to vitamin B_{12} Megaloblastic anaemia of transient nature may occur in infants in association with diarrhoea and vomiting and may respond poorly to both folic acid and vitamin B_{12}

Other Anaemias Due to Defective Erythropoiesis

As a result of nutritional experiments in animals various factors have been postulated as being necessary for erythropoiesis The chief of these are the metals copper and cobalt and the vitamins pyridoxine riboflavin and nicotinic acid There is no convincing evidence that they play any part in erythropoiesis in man apart from the fact that cobalt is contained *in the vitamin B_{12} molecule* Haematinic factors seem to be very species specific as is shown conversely by the failure to produce pernicious anaemia *in animals Vitamin C probably* does act as a factor in human erythropoiesis but undoubtedly part of the anaemia of scurvy which is of normocytic type is due to haemorrhage Deficiency of thyroxine also causes a normocytic anaemia *Persons with myxoedema may* have normocytic anaemia with an haemoglobin level of about 8 g/100 ml which responds to treatment with *thyroid extract alone Gross* defect of dietary protein may cause anaemia this is very rare in Britain but common in Africa in association with pregnancy

Anaemias Due to Depression of Erythropoiesis

The anaemia of infection is the most important example of this group Many persons with a severe acute *septic process develop* marked anaemia Those infected by haemolytic organisms may show evidence of increased blood destruction but as a rule there is a normocytic or microcytic anaemia without reticulocytosis or hyperbilirubinaemia and with normal levels of leucocytes and platelets *The mar*

row is normal or hyperplastic and contains haemosiderin even though the serum iron is often reduced In such cases the erythrocytes can be shown to contain an excess of protoporphyrin The mechanism of the anaemia is thought to be a failure of iron to unite with protoporphyrin Minor degrees of anaemia of this type are as common as iron deficiency anaemia Haematinics are quite ineffective and severe cases can be treated only by blood transfusion Similar anaemia may accompany malignant disease and chronic nephritis in which in some instances increase in plasma volume occurs Some patients may nevertheless have very high blood urea levels for a considerable time without becoming anaemic However estimation of blood urea is often of value in unexplained anaemias

Haemolytic Anaemias

Anaemias due to increased haemolysis can be classified into those in which the actual haemolysis is an abrupt process and those in which it proceeds more or less continuously

Sudden Massive Haemolysis

When haemolysis is abrupt haemoglobin appears in the urine In severe cases there is often in addition pain in the loins headache rigors pyrexia and circulatory collapse which may lead on to acute tubular necrosis with oliguria or even anuria Initially there is a sharp reduction in the number of erythrocytes and free haemoglobin or methaemalbumen appear in the plasma Later hyperbilirubinaemia develops often with frank jaundice After a day or so nitrogen retention sets in the severity of which depends on the degree of oliguria The blood does not regenerate until the renal condition has recovered a reticulocytosis then occurs This syndrome is rare and if untreated often fatal It may be caused by incompatible blood transfusion and in the tropics by blackwater fever (*see* p 108)

Treatment If there is severe collapse or anaemia an initial transfusion of compatible blood should be given During the stage of oliguria fluid balance must be carefully maintained and if there is anuria the fluid intake should be 750 ml a day This can be given by gastric tube with 400 g of glucose Vomit should be returned to the gastric drip after filtering through gauze If gastric feeding is very troublesome it is best abandoned and 40 per cent glucose by polythene catheter given instead into the inferior vena cava a smaller vein would become thrombosed The high calorie intake is given in an endeavour to keep the blood urea and plasma potassium as low as possible In severe cases dialysis with an artificial kidney machine may be necessary When diuresis sets in after 7 to 10 days the intake of both water and salts should be carefully correlated with the output as the recovering kidneys have at first no concentrating power and hypokalaemia may rapidly succeed hyperkalaemia It has recently been reported that cortisone is effective in blackwater fever

Moderate Intermittent Haemolysis

Less severe intravascular haemolysis is caused by the paroxysmal haemoglobinurias in which there are no renal complications

1 *Haemoglobinuria from Cold* This very rare disorder usually occurs in syphilitics Recurrent attacks occur on exposure to cold in which there is pain in the back cramps and rigors followed by the passage of clear port wine-coloured urine Some anaemia may develop The activation by cold of the responsible haemolysin can be demonstrated by the Donath Landsteiner reaction Treatment of the attacks is symptomatic

2 *Paroxysmal Nocturnal Haemoglobinuria (Marchiafava Micheli Syndrome)* A rare disease of adults Haemoglobinuria usually slight occurs at night It is due to an increased susceptibility of the erythrocytes for normal haemolysins present in plasma The activity of the haemolysins is enhanced by the slight acidosis which occurs at night when gastric secretion is reduced Diagnosis is made by Ham s test which demonstrates lysis of susceptible cells by acidified normal serum There is marked anaemia reticulocytosis hyperbilirubinaemia and haemosiderinuria The disease process persists indefinitely and uninfluenced by treatment but the expectation of life is not greatly reduced

3 *Haemoglobinuria from Exertion (March Haemoglobinuria)* This condition occurs in young adult males as a result of strenuous exercise There are no blood changes or constitutional symptoms Spontaneous recovery occurs

Haemolytic Anaemias in which the Haemolytic Process is Continuous

Haemolytic anaemias in which haemolysis is insidious are accompanied by some degree of jaundice without bilirubinuria Splenomegaly is usual in chronic cases The blood shows a continuous reticulocytosis and a tendency to a macrocytosis as reticulocytes are larger than mature erythrocytes Increased blood destruction is shown by increased faecal stercobilinogen It may also be demonstrated

by the use of erythrocytes labelled with radio active chromium but this is unnecessary in practice Increased urinary urobilinogen occurs but is also found in disease of the liver The marrow is hyper plastic with many normoblasts

Toxic Haemolytic Anaemias

Some infections notably malaria streptococcal septicaemia and those due to *Cl welchii* cause haemolytic anaemia Other causes include drugs and chemicals such as phenylhydrazine sulphonamides sulphones primaquine lead arsine dinitrobenzene toluenediamine snake venoms and also severe burns In lead poisoning the anaemia is not a promi nent feature with only slight reduction in haemo globin reticulocytosis of about 5 per cent and the characteristic punctate basophilia or stippled ery throcytes which are however not pathognomonic Many haemolytic anaemias due to drugs are charac terized by the presence in the corpuscles of refractile objects known as Heinz bodies

Congenital Haemolytic Anaemias

(a) Due to Defective Cell Structure Familial Acholuric Jaundice (Hereditary Spherocytosis) This disease is transmitted as a Mendelian dominant affecting both sexes equally The essential defect seems to be a failure of the erythrocyte cell membrane to metabolize glucose correctly The cell in consequence becomes unduly spherical in which shape it is more susceptible to haemolysis These spherocytes can be seen in blood films and have an increased fragility in hypotonic saline The symptoms may appear soon after birth and may be trivial there being no more than slight jaundice and splenomegaly Leg ulceration occasionally occurs There may be periodical crises when the anaemia becomes more profound and the patient feverish These crises are now thought to be due to periodic phases of marrow aplasia which cannot be tolerated because the erythrocytes have a life span of only some 15 days The normal person on the other hand whose erythrocytes survive for 120 days is unaffected by similar phases of marrow aplasia Pigment gallstones may be caused by the increased excretion of bilirubin Treatment by splenectomy almost always produces clinical cure but the ery throcytes remain spherocytic

There are rare cases of congenital haemolytic anaemia similar to congenital acholuric jaundice but without spherocytes or increased saline fragility

(b) Due to Defective Haemoglobin Formation These diseases are inherited as Mendelian recessives The heterozygous patient shows a mild form with little or no clinical disability called the trait while the homozygous patient has a more severe disease which may be fatal in childhood The treatment is symptomatic splenectomy being ineffective

Thalassaemia (Cooley s Anaemia or Mediterran ean Anaemia) This occurs in persons of Mediter ranean stock and is due to an inability to form normal haemoglobin in sufficient amount. The haemoglobin present is a mixture of Haemoglobin A found in normal persons and Haemoglobin F nor mally present in the foetus There is an haemolytic anaemia with low MCHC many target cells and decreased saline fragility The target cell is an abnormally flat cell which in stained films seems to have central and outer well stained zones and an intermediate colourless zone Persons with the trait have target cells but very slight anaemia The homo zygous patient has a severe anaemia with skeletal changes and usually dies in childhood

Sickle cell Anaemia This condition occurs in negroes Up to 15 per cent show the trait which merely consists of the phenomenon of erythrocyte sickling and causes no disability apart from a ten dency to thromboses when exposed to low oxygen tensions such as by high altitude flying The defect consists of an abnormal haemoglobin Haemo globin S which can be demonstrated by electro phoresis This crystallizes in the reduced form thus producing in erythrocytes exposed to low oxygen tensions peculiar shapes like sickles The homo zygous disease is severe and invariably fatal in child hood It may give rise to fever thromboses and cardiac symptoms

Other anaemias due to haemoglobins giving abnormal electrophoretic mobilities (Haemoglobins C D E etc) are found almost invariably in Afri cans or Asians Target cells are found but the homo zygous form of the disease is not usually severe A moderately severe disease can also be produced if one parent is affected with the sickle cell or Haemo globin C trait and the other the thalassaemia trait both genes being transmitted to the same child

Haemolytic Anaemias due to Haemolysins

Auto Immune Haemolytic Anaemia (Acquired Acholuric Jaundice)

This condition is caused by the presence in the blood of haemolytic antibodies for the patient s own erythrocytes They may be either non specific when they affect all types of human erythrocytes or specific when they react with all cells possessing a certain blood group antigen which is also present in the patient s cells such as the antigen E of the Rh system Why an antibody should be produced to a factor the patient himself possesses *is not understood* The illness may be of acute onset with marked fever

rapidly developing anaemia and jaundice or it may be more chronic and afebrile The patient in con trast to the subject of familial acholuric jaundice is more sick than icteric The blood shows anaemia often macrocytic with reticulocytosis and occa sionally a few normoblasts leucocytosis is common The erythrocytes show an increased saline fragility and are spherocytic as in the familial disease but in addition haemolytic antibody is adsorbed on to their surface which may be demonstrated by the direct Coombs test. This test depends on the fact that the adsorbed antibody consists of human globu lin and such cells washed free of suspending plasma are unlike normal erythrocytes agglutinated by an anti human globulin serum which is itself made by injecting human globulin into a rabbit In addition evidence of antibody formation may be found in the serum which may manifest itself by difficulty in cross matching blood for transfusion In some cases the condition is associated with high titre cold agglu tinins when compatible erythrocytes are agglutinated by the patient s serum at refrigerator tempera ture The condition may be idiopathic but also complicates other diseases The most notable of these are diseases of lymph glands such as lympho sarcoma and lymphatic leukaemia when the mech anism for the production of antibodies is probably deranged ovarian dermoid cysts and following virus pneumonia in which high titre cold agglutinins are usually found Sometimes the condition rapidly improves particularly in the acute cases and per manent recovery results This is often rightly or wrongly attributed to blood transfusion In other cases blood transfusion may be made difficult by the absence or rarity of apparently compatible blood and the transfusion itself accompanied by febrile reactions A remission which may be perma nent can often be induced by steroid drugs such as prednisone 50 mg orally a day or cortisone 200–300 mg orally a day If a remission is not obtained or relapse occurs on stopping the hormone splenectomy should be carried out This is often effective but is not so uniformly successful as in the familial disease

Erythroblastosis Foetalis

This is a haemolytic anaemia peculiar to the new born It is due to a blood group antigen present on the foetal erythrocytes inherited from the father entering the maternal circulation and stimulating the production there of an antibody as the par ticular antigen concerned is not represented on the maternal erythrocytes The antibody then passes back into the foetal circulation and combines with the antigen present on the foetal erythrocytes thus causing haemolytic anaemia which is the essential feature of the disease Since mother and foetus rarely have identical blood group antigens it must be wondered why nearly all foetuses do not develop erythroblastosis In particular since Group O women already possess α and β agglutinins before pregnancy it might seem that all group A and B foetuses of Group O mothers would be affected The reason why this does not happen at any rate to any marked extent seems to be that naturally occurring antibodies do not cross the placental barrier However Landsteiner (ABO) group incom patibility between foetus and mother may cause some abortions at one to three months and in a few instances true erythroblastosis

The vast majority of cases of erythoblastosis foetalis are due to antibody developing to the D antigen of the Rh group The presence or absence of this antigen determines whether a person is Rhesus positive or negative in ordinary parlance The D antigen is antigenically more active than the majority of other blood group antigens apart from the Landsteiner group and in addition owing to its frequency (85 per cent of the population of Britain being Rh positive) maternal foetal incompatibility is likely to be common Yet only 1 in 22 marriages of Rh positive men and Rh negative women results in one or more affected children This is either because foetal erythrocytes rarely penetrate into the maternal circulation or because if they do so penetrate they are usually destroyed before exerting any antigenic effect Rh negative mothers who have previously had a transfusion or injection of Rh positive blood are especially likely to produce anti bodies When Rhesus antibody develops however it always penetrates back into the foetal circulation and causes erythroblastosis provided it is of suf ficient strength and the foetus is Rh positive During parturition foetal blood probably penetrates the maternal circulation as erythroblastosis is very rare in first pregnancies

The affected foetus may die *in utero* just before term and is born macerated with an enlarged spleen hepatic cirrhosis and a voluminous pink placenta When oedema and serous effusions are marked the condition is described as *hydrops foetalis* Rhesus incompatibility is not however a cause of early miscarriage If the baby is born alive it is said to have *icterus gravis neonatorum* unless it has hy drops It may at first appear normal but the vernix caseosa is typically a golden colour Jaundice rapidly develops and the infant may become pro gressively weaker from anaemia If the jaundice is severe the bilirubin may be adsorbed on to various parts of the brain notably the basal ganglia which become stained a marked orange a condition called kernicterus This causes twitching and later coma and if not fatal the infant may suffer permanent

cerebral damage leading to mental defect spasticity or athetosis The essential cause of kernicterus is the failure of the immature liver to excrete the large amount of bilirubin produced This has a greater affinity for nervous tissue than has post hepatic bilirubin (characteristic of obstructive jaundice) or jaundice due to liver disease The anaemia is often accompanied by large numbers of nucleated erythrocytes which give the disease its name There is a reticulocytosis above the normal 5–10 per cent at birth The erythrocytes give a positive direct Coombs test If untreated some infants gradually recover as the maternally derived antibody becomes exhausted Some survivors have permanent nervous damage and others green pigmentation of the teeth After one foetus has been affected subsequent pregnancies result in foetuses which if they are Rh positive tend to be progressively more seriously affected

The prophylactic treatment is to avoid the transfusion or intramuscular injection of Rh positive blood into all Rh negative females who may subsequently have children Expectant mothers should have their blood grouped early in pregnancy and if Rh negative tested for antibodies again at 34 weeks gestation If antibodies are found the mothers should be allowed to go to term and delivered in a hospital specializing in such cases Examination of the father s blood to see whether he is homozygous or heterozygous Rh positive is useful for prognosis as if he is heterozygous only half the children will be Rh positive Immediately after the birth the cord blood should be collected and the group direct Coombs test haemoglobin and bilirubin determined If the Coombs test is positive and either the haemoglobin below 14 8 g/100 ml or the bilirubin above 2 7 mg per cent exchange transfusion should be carried out with Rh negative blood A plastic catheter is inserted into the umbilical vein and 20 ml of blood is alternatively aspirated and injected until 500 ml has been used This must be done within a few hours of birth before the vein closes The treatment is highly effective Subsequent transfusions are seldom required the incidence of kernicterus is reduced and the mortality falls from over 20 per cent to under 5 per cent If facilities are not available or the umbilical vein has closed simple transfusion of up to 200 ml of blood may be given This may have to be repeated and does not affect kernicterus If there is a history of previous severe erythroblastosis induction of labour at the 36th week may enable an infant to be treated before the disease process is fully developed Induction of labour as a routine in all mothers with antibodies may on the other hand cause some slightly affected infants to succumb to prematurity

Haemorrhagic Disorders

Haemorrhagic disorders include those diseases in which there is a tendency to bleed spontaneously or after trivial trauma which may be called a haemorrhagic diathesis They may be divided into two main groups the purpuras and the coagulation defects Purpuras are characterized by petechial haemorrhages superficial bruising and oozing from mucous surfaces Petechial haemorrhages can be distinguished from minute telangiectases by pressing with a glass slide when the latter disappear as the blood is squeezed out of the vessels In the coagulation defects there are deep seated haemorrhages but no petechiae These haemorrhages result from injury but the bleeding is out of all proportion to the amount of trauma Haemarthroses are common but bleeding from apparently intact mucous membranes as in the purpuras is rare It is thus possible in many cases to differentiate between the purpuras and coagulation defects on clinical grounds alone

Purpuras are due to a defect in the mechanism of haemostasis This is normally effected by contraction of the damaged capillaries and blockage of the cut-end of the vessels by a mass of platelets Valuable tests in the diagnosis of the purpuras are the *capillary resistance test* and the *bleeding time* To perform the capillary resistance test a sphygmomanometer cuff is placed round the arm inflated to 40 mm of mercury and left *in situ* for 15 min The appearance of more than 6 petechiae in the antecubital fossa indicates a positive test The bleeding time is the time taken for a simple needle puncture to stop bleeding It can be assessed in various ways but whatever method is used the results are not always consistent in the same patient The number and morphology of the circulating platelets and of their precursors in the marrow the megakaryocytes may also require study Finally substitution of the patient s platelets in the thromboplastin generation test assesses their functional capacity

The coagulation mechanism which comes into action after the haemostatic process is complex and imperfectly understood The following tentative scheme explains at least some of the observed facts Clotting can be presumed to occur in a number of stages—

1 Contact with a water wettable substance causes disintegration of *platelets* The substance

formed reacts with *antihaemophiliac globulin* and *Christmas factor* to form tissue thromboplastin or *prothromboplastin*

2 Prothromboplastin is converted into *active thromboplastin* by means of *factors V and VII* in the presence of *calcium ions*

3 Active thromboplastin converts *prothrombin* into *thrombin* in the presence of *calcium ions*

4 Thrombin converts *fibrinogen* into *fibrin*

The number of platelets required in stage one is so small that in practice a platelet deficiency does not cause a coagulation defect This is also never due to simple calcium deficiency

The laboratory tests employed in studying coagulation defects are—

1 *The Clotting Time or Whole Blood Coagulation Time* This simply measures the time taken for blood to clot under standard conditions

2 *The One Stage Prothrombin Time* Calcium ions are added to a mixture of tissue thromboplastin (dried brain suspension) and patient s plasma and the clotting time is measured This time is prolonged in deficiencies of prothrombin and factors V and VII and also in hypofibrinogenaemia The normal varies with each batch of reagents and is therefore expressed either as a prothrombin index or concentration These are both arbitrary figures obtained by reference to the prothrombin time of a normal plasma

3 *The Two stage Prothrombin Time* The amount of actual thrombin produced is measured This is assumed to be proportional to the amount of prothrombin present

4 *Thromboplastin Generation Test* Platelets aluminium hydroxide absorbed plasma (containing antihaemophiliac globulin and factor V but no prothrombin) and serum (containing Christmas factor and factor VII) are mixed with calcium ions At one minute intervals samples of the mixture and further calcium are added to normal plasma The clotting times of these final mixtures are then proportional to the amount of thromboplastin generated in the original mixture

Purpuras

1 Those in which the platelets are unaffected and the bleeding time is normal but the capillary resistance test may be positive

Schonlein Henoch Syndrome

This affects children and young adults The condition is thought to be allergic There is a purpuric rash characteristically on the backs of the elbows and on the buttocks and ankles There may be abdominal colic and melaena or periarticular swellings associated with pain and tenderness and occasionally haematuria There are no characteristic blood changes The prognosis is good though relapses may occur The treatment is symptomatic except in severe cases when steroids may be used

Senile Purpura

Flat superficial ecchymoses up to an inch or so across occur on the extensor surfaces of the forearms of the elderly This condition is extremely common Treatment is not required

Simple Symptomatic Purpura

Petechial haemorrhages may develop in the course of many fevers such as meningococcal meningitis formerly referred to as spotted fever In some cases there is an associated platelet defect but many are due simply to capillary damage

Scurvy

This disease due to lack of vitamin C is considered on page 161

2 Purpuras in which the platelets are reduced and the bleeding time prolonged

Essential Thrombocytopenia (Purpura Haemorrhagica)

This occurs at all ages but is most common in young adults There are two main forms of the disease acute and chronic In the acute form there may be an abrupt onset with a petechial rash superficial ecchymoses and haemorrhages from the alimentary and uro genital tracts and a moderate degree of fever Death may occur from anaemia or cerebral haemorrhage though some cases spontaneously recover and others become chronic In the more common chronic form crops of petechiae and bruises occur periodically often with considerable intervals of freedom About one case in three has slight splenomegaly There is little anaemia and the only specific feature is thrombocytopenia usually to below 50 000 platelets per mm^3 The bone marrow is normal and there are numerous megakaryocytes In some cases platelet antibodies have been demonstrated and the defect in the platelets is now thought to be analogous to that of the erythrocytes in acquired acholuric jaundice

The treatment in an acute case consists of transfusion to control anaemia but unless fresh blood (preferably collected in siliconed apparatus) is used this will not affect the platelet count The efficacy of transfusions of platelet containing blood is of short duration and they should be reserved for acute cases Splenectomy is effective in the majority of chronic cases Steroids such as prednisone 50 mg

a day or cortisone 200-300 mg a day by mouth produce temporary improvement in about half of those treated Treatment may be continued for months and the dose gradually reduced to as low a level as possible

Symptomatic Thrombocytopenia

This may occur during the course of other blood diseases typically leukaemia and aplastic anaemia and to a lesser extent in pernicious anaemia It also follows exposure to chemicals such as benzol and the use of drugs such as chloramphenicol sulphonamides arsenicals gold tridione and phenylbutazone In many of these cases megakaryocytes are absent from the marrow but in others where there may be a sensitization effect as opposed to direct destruction they may be increased A typical example of this is purpura due to sedormid in which lysis of platelets from a susceptible subject occurs *in vitro* if the drug is added to the blood

Miscellaneous Conditions in which Haemostasis is Abnormal

1 *Constitutional Thrombopathy* (Von Willebrand s Disease or Hereditary Pseudohaemophilia) A rare hereditary disease in which the clinical findings resemble a coagulation defect but in which a moderate deficiency of antihaemophiliac globulin is associated with a prolonged bleeding time The platelets are normal both in number and morphology There is no effective treatment

2. *Haemorrhagic Thrombasthenia (Glanzmann s Disease)* A rare hereditary disease of males and females clinically resembling thrombocytopenic purpura The platelets though normal in number show morphological abnormalities and are ineffective when substituted for normal platelets in the thromboplastin generation test There is no effective treatment

3 *Hereditary Haemorrhagic Telangiectasia* A not uncommon condition affecting both sexes in which small telangiectases may be seen in the nose and on the lips and tongue Others internally may give rise to gastro intestinal bleeding and a consequent rather intractable iron deficiency anaemia result Haematuria may also occur Treatment consists of iron for the anaemia but recently it has been suggested that oestrogens may prevent further bleeding

Conditions in which the Coagulation Mechanism is Defective

Haemophilia (Haemophilia A)

This disorder is hereditary and is transmitted by a sex linked recessive gene carried on the X chromosome Males normally suffer from the disease as in them the gene on their one X chromosome is not inhibited by the smaller Y chromosome None of a male haemophiliac s sons is either affected or transmits the disease but all his daughters are carriers and half their sons have the disease and half their daughters carry it Half the daughters of a marriage between a haemophiliac man and a carrier woman will be haemophiliacs as they will be homozygous with an affected X chromosome from each parent Until recently no authentic case of haemophilia in women had been described About 25 per cent of cases arise spontaneously and have no family history

The defect consists of lack of antihaemophiliac globulin which is a labile substance rapidly disappearing from stored blood The majority of cases have an increased coagulation time but in some it is within the normal range The one stage prothrombin time is always normal as the brain thromboplastin used in this test is really prothromboplastin and contains the equivalent of antihaemophiliac globulin The thromboplastin generation test shows defective generation when the patient s aluminium hydroxide absorbed plasma is used This test is more sensitive than the coagulation time and in addition differentiates haemophilia from Christmas disease

Haemophilia usually manifests itself in the second or third year there being no haemorrhages at birth from the umbilical cord Large deep seated haemorrhages characteristically occur as an excessive response to trauma There may be haematuria melaena or haemorrhage into the spinal theca with resultant compression of the cord A common type of haemorrhage is haemarthrosis which may be followed by incomplete absorption and permanent limitation of movement Cases differ considerably in severity and both the coagulation time and the clinical state fluctuate Some cases may have almost always a normal coagulation time and yet suffer excessive haemorrhage

The specific treatment consists of the intravenous administration of antihaemophiliac globulin This is impossible to obtain commercially as human antihaemophiliac globulin requires large amounts of fresh plasma for its preparation and that from animals is antigenic in man A similar effect may be obtained with freshly frozen plasma or fresh citrated blood both of which contain antihaemophiliac globulin though several pints may be required to arrest bleeding Effective local treatment consists in the application of thrombin solutions or Russell viper venom 1 1000 (Stypven) together with the application of packs In haemorrhage from the gum after tooth extraction padded dental splints

should be applied as suturing the gum may result in blood tracking into the neck All surgical procedures should be avoided as far as possible and when they are absolutely necessary fresh blood or plasma should be given prophylactically Before major operations exchange transfusion has been successfully used 20–30 pints of fresh blood are run into one of the patient s veins while a similar amount is being simultaneously removed from another vein

Christmas Disease (Haemophilia B)

This condition has recently been separated from haemophilia The first patient studied was called Christmas The inheritance and symptomatology are the same as in haemophilia and the laboratory findings similar except that in the thromboplastin generation test there is defective generation when the patient s serum is substituted for normal serum The defective substance is called Christmas factor This is moderately stable in stored blood and therefore specific treatment does not require absolutely fresh blood for transfusion

Plasma Thromboplastin Antecedent Deficiency

This disease has recently been recognized in America Clinically it resembles mild haemophilia The only laboratory abnormality is deficient thromboplastin generation partially corrected when either normal serum or aluminium hydroxide absorbed plasma are used

Miscellaneous Coagulation Defects

Following the therapeutic use of heparin which is an antithrombin and in a few rare cases where there are spontaneous circulating anti-coagulants syndromes may be seen similar to haemophilia but of abrupt onset in later life The coagulation defect pattern is varied The nature of the disorder can often be demonstrated by adding patient s alumina (aluminium hydroxide absorbed) plasma as well as normal alumina plasma in the thromboplastin generation test Thromboplastin formation is found to be decreased as the patient s plasma *inhibits* normal coagulation

Conditions in which the One stage Prothrombin Time is Prolonged

Until recently all these conditions apart from fibrinogen deficiencies were grouped together as the prothrombin deficiencies The modern two stage prothrombin estimation which measures that substance only and qualitative tests for deficiencies of factor V and VII are enabling us to classify them more precisely If aluminium hydroxide treated normal plasma in small quantities corrects to nearly normal a plasma with a prolonged one stage prothrombin time that plasma has a deficiency in factor V If it is corrected by small amounts of serum the defect is that of factor VII Similar results are obtained in the thromboplastin generation test which is normal in true prothrombin deficiency The coagulation time is sometimes prolonged and the one stage prothrombin time is always increased in these conditions This differentiates them from haemophilia and related conditions in which the coagulation time is usually prolonged but the one stage prothrombin time is always normal The symptomatology of both groups of conditions is essentially the same while congenital forms of prothrombin factor V and factor VII deficiency have been described Factor VII is the principal defect resulting from treatment with anti coagulants of the warfarin sodium phenindione type

Prothrombin is produced by the liver as a result of the action of fat soluble vitamin K which is synthesized by intestinal bacteria Consequently prothrombin deficiency may occur in liver disease steatorrhoea obstructive jaundice and in neonates before the intestines have been colonized by bacteria

Haemorrhagic Disease of the Newborn This condition manifests itself by gastro intestinal haemorrhage hence its alternative name of melaena neonatorum Haemorrhage may also occur from the umbilicus and other sites The bleeding starts abruptly between the first and fifth days and the condition occurs about once in four hundred births Treatment which is usually effective consists of one intramuscular injection of 2–5 mg of synthetic vitamin K This dose should not be exceeded particularly in premature infants as total dosage of the order of 30 mg is thought to increase considerably the likelihood of kernicterus of prematurity which arises independently from erythroblastosis Blood transfusion is often also required particularly if there has been much blood lost If a previous baby has been affected satisfactory prophylaxis is obtained if the mother is given the vitamin just before delivery

Fibrinogen Deficiencies A haemorrhagic state may be caused by the absence or diminution of the plasma fibrinogen If it is completely absent the plasma is incoagulable even on the addition of thrombin if it is diminished there is some increase in coagulation time and one stage prothrombin time Rare congenital cases are met with but acquired hypofibrinogenaemia is becoming increasingly recognized in cases of liver disease prostatic carcinoma and concealed accidental haemorrhage of pregnancy It may also follow massive

infusions of dextran Temporarily effective treatment consists of the intravenous administration of two or more grammes of fibrinogen or of dried plasma reconstituted in the minimum amount of sterile water the fibrinogen present in stored blood is in too dilute a solution to raise effectively the concentration in the patient s blood

Bleeding History before Operation

The problem often arises as to what measures to adopt in a patient who gives a history of bleeding and who is due for a surgical operation This usually takes the form of one or more episodes of bleeding after dental extraction or tonsillectomy and a statement that he bruises easily In assessing such cases the history is all important and answers to the following questions are of help Is bleeding from cuts prolonged for days or merely unusually profuse? Do other members of the family particularly maternal uncles bleed easily? Have petechiae or deep haemorrhages ever been noticed rather than superficial bruises? Have there been any operations which have not led to bleeding? Has the bleeding necessitated transfusion? If clinical assessment on this basis suggests that there is reason for suspecting a haemorrhagic diathesis the case should be investigated Capillary resistance test bleeding time and leucocyte and platelet counts should be done if a defect of haemostasis is suspected and coagulation time one stage prothrombin time and thromboplastin generation test if a coagulation defect is suspected Cases without a definite history cannot in practice be so thoroughly investigated as the methods are too time consuming A less tedious series of investigations such as the mere determination of bleeding and clotting times will not exclude haemorrhagic diatheses

Aplastic Diseases

These include certain anaemic states agranulocytosis and thrombocytopenia and may occur singly or in combination The first two are considered below thrombocytopenia is described under haemorrhagic disorders When erythrocytes leucocytes and platelets are reduced concurrently the condition is known as aplastic anaemia

Aplastic Anaemia

The syndrome may be idiopathic or acquired It occurs industrially from benzene and its derivatives such as trinitrotoluene and following the use of drugs such as arsenicals sulphonamides gold and tridione The most important drug in this respect is chloramphenicol although only a very few of the large number of persons treated with it develop aplastic anaemia It is more common in children possibly because they tend to be given a relatively larger dose of chloramphenicol Other causes include excessive irradiation certain infections (such as miliary tuberculosis) and replacement of the bone marrow by other tissue (such as in aleukaemic leukaemia metastatic carcinoma multiple myeloma and osteosclerosis) Aplastic anaemia due to replacement of the marrow can at least at autopsy be easily distinguished from the idiopathic variety but when the condition follows the use of drugs there is often uncertainty as to whether or not the drugs were responsible The bone marrow in severe cases other than those due to marrow replacement is fatty Marrow puncture reveals few cells of all elements but sections are required to demonstrate the excessive fat. In some cases marrow examination shows no diminution in cellularity this is partly because the lesions may be patchy but sometimes there seems to be either a failure of cell maturation or of the mechanism of release of cells into the general circulation There is usually normocytic but occasionally a macrocytic anaemia the erythrocytes show some anisocytosis but less so than in pernicious anaemia of corresponding severity In spite of the nature of the disease the reticulocytes may be as high as 5 per cent There is leucopenia often of the order of 1 000 cells per mm^3 with the granulocytes chiefly affected There are varying degrees of thrombocytopenia

The symptoms are those of anaemia appearing insidiously with in addition petechial haemorrhages and bleeding from various sites (such as the gums and gastrointestinal and urogenital tracts) The leucopenia may result in necrotic ulcers principally in the mouth Apart from petechiae there are no significant physical signs and the spleen is not palpable Except on the few occasions when a fatty marrow can convincingly be demonstrated by histological section of aspirated material the diagnosis must be made by exclusion of marrow replacement conditions and aleukaemic leukaemia

The treatment consists in repeated blood transfusion preferably of concentrated cells derived from blood as fresh as possible The transfusions should be given frequently at the start so as to raise the haemoglobin to 12 g/100 ml or more and repeated when it falls to 9 g/100 ml In certain cases it may be preferable to give about one pint of blood regularly once a week this may prevent hospitalization and allow the maximum activity Care must be

taken with cross matching the blood as repeated transfusions are liable to lead to the formation of atypical antibodies Some cases make a spontaneous recovery after leading a transfusion life for years

Conditions closely related to aplastic anaemia are pure red-cell aplasia and hypersplenism Pure red cell aplasia affecting children is known as congenital hypoplastic anaemia or erythrogenesis imperfecta this rare disease manifests itself soon after birth Treatment is by repeated transfusions while splenectomy may be of value but the condition tends to improve as the child gets older In adults red-cell aplasia has chiefly been reported in connexion with thymic tumours A type of aplastic anaemia occurring in association with an enlarged spleen and a cellular marrow is benefited by splenectomy This is known as hypersplenism as the spleen is thought to produce an inhibition of marrow function it may be idiopathic or follow enlargement of the spleen due to some other cause such as sarcoidosis Gaucher s disease or Hodgkin s disease

Agranulocytosis

By this term is meant a virtual disappearance of polymorphonuclear leucocytes from the peripheral blood with no alteration in the erythrocytes or platelets It also may be idiopathic or secondary The secondary variety is by far the more common and usually follows the use of certain drugs The most important of them used to be amidopyrine but because it often caused agranulocytosis it is now rarely prescribed A dose of about 1–2 g may cause sensitization in a susceptible subject after which as little as 0 2 g will precipitate an attack of agranulocytosis Other important drugs are sulphonamides usually when the total dose is more than 30 g thiouracil and its derivatives phenylbutazone and tridione Many others such as arsenicals dinitrophenol and gold have been implicated Agranulocytosis may also occur in severe infections

The symptoms are typically fever up to 104 F malaise and sore throat The latter usually proceeds to an ulcerating membranous lesion which may involve tonsils gums and palate Later death may follow as a result of septicaemia or pneumonia In a few cases there may be ulcerating lesions elsewhere such as the vulva or the conjunctiva All these lesions should be regarded as infections to which no resistance is possible owing to the dearth of leucocytes The blood shows so few polymorphs that diagnosis is not in doubt the polymorph counts range from 0–300/mm³ The lymphocytes may or may not be reduced The bone marrow shows in some cases a virtual absence of leucocytic elements in others intact myelocytes and myeloblasts may be seen possibly indicating a maturation defect or the start of recovery In either case the prognosis is better than when there are no leucocytic elements

The treatment is to give antibiotics to combat infection Penicillin in dosage of at least one mega unit a day is the most valuable and should always be used unless there are penicillin resistant organisms when it may be replaced by streptomycin or one of the tetracyclines Pyridoxine intravenously 50–200 mg daily and steroids have been claimed to be of use on the basis of isolated recoveries The mortality is appreciable whatever the treatment the aim of which is to stave off death by preventing infection until spontaneous recovery occurs

Various sub varieties of agranulocytosis have been described Cyclical neutropenia presents as neutropenia recurring regularly every three weeks with mild fever and sore throat it has started in children and adults and usually persists for years Primary splenic neutropenia consists of neutropenia associated with splenomegaly and active myeloid cells in the marrow It is a variant of hypersplenism and may be cured by splenectomy

Agranulocytosis may be avoided by not using drugs of the amidopyrine group and by using sulphonamides in modest doses only but drugs like thiouracil tridione and phenylbutazone to be effective must be continued for a long period There is however no evidence that performing periodic leucocyte counts in any way gives warning of impending agranulocytosis Patients should be told to stop the drug and report to a doctor on the first sign of a sore throat or fever when it can then be quickly ascertained whether in fact there is agranulocytosis

Effect of Ionizing Radiations

These include all types of irradiations from nuclear weapons to diagnostic and therapeutic X rays When the atomic bombs were dropped on Hiroshima and Nagasaki three main clinical groups of haematological effects were noticed Agranulocytosis developed within a few days and led to death within three weeks Within three to five weeks of exposure haemorrhages from various sites developed accompanied by thrombocytopenia with or without the development of circulating anti-coagulants of the heparin type Aplastic anaemia started five to seven weeks after exposure and was characterized by erythrocyte counts as low as one million/mm³ These effects are related to the time the adult cellular elements remain in the circulation the radiation damages the marrow not the peripheral blood which remains

apparently normal until effete cells fail to be re placed Aplastic anaemia has been noted in girls painting the dials of luminous watches who were in the habit of pointing the brushes in their mouths In patients undergoing intensive radiotherapy par ticularly that directed against widespread bony lesions there is often a leucopenia of about 2 000 leucocytes the lymphocytes being more affected than the polymorphs This usually returns to normal in a few weeks after treatment ceases though extreme leucopenia may persist and indi cates the possibility of more serious damage There is evidence that irradiation may have a stimulating effect and lead to leukaemia in certain individuals The incidence of leukaemia in persons who have been previously treated by X rays for ankylosing spondylitis is greater than in the general population as it is in the children of mothers who have had diagnostic pelvic X ray examinations in pregnancy

When people are liable to be exposed to irradia tion in the course of their work harmful rays should be prevented by physical methods from reaching them This is effected by impermeable screens protective clothing and the handling of radio active isotopes with tongs activated by remote control In atomic energy establishments the effi cacy of such methods is controlled by measuring both the free irradiation present in the various departments and the dose each individual receives by exposure meters carried on the person In this way it can be guaranteed that each worker is not exposed to a harmful degree of irradiation The amount of irradiation which will give rise to mini mal changes in the blood is much larger than the dose permitted and the performance of periodical blood counts is an insensitive method of detecting an excessive degree of exposure In X ray depart ments exposure meters are used to determine the amount of irradiation each member of the staff has received and it is recommended that blood counts at three monthly intervals should be done if any one has been exposed to more than half the maxi mum permitted weekly dose as averaged over three months

Leuco-erythroblastic Anaemia (Myelophthisic Anaemia)

This term denotes an anaemia characterized by the presence of undue numbers of myelocytes and erythroblasts in the peripheral blood Myelocytes are often found in small numbers in any marked leucocytosis but in this condition they are more noticeable than the increase in total count Similarly normoblasts may be found in the peripheral blood in any severe anaemia particularly when associated with a high reticulocyte count but here they are found even when the haemoglobin is only slightly diminished and the reticulocytosis insignificant. In addition the type of normoblast found is often un usually primitive The anaemia which may be either normocytic or macrocytic is in general a manifesta tion of extramedullary haemopoiesis It represents a return to the state of affairs in the foetus when the peripheral blood contains nucleated cells and may be due to stimulation of part of the bone marrow with destruction of the remainder It can occur in carcinomatosis of bone Gaucher s disease and myelomatosis the characteristic cells of these conditions may be revealed by marrow puncture This kind of anaemia also occurs in osteopetrosis and myelosclerosis but not in other generalized bony disease such as osteitis deformans Osteo petrosis or the marble stone disease of Albers Schonberg is considered on page 534

Myelosclerosis is a rare disease of adults charac terized by fibrosis of the bone marrow There is no tendency to fractures and no definite distinctive X ray appearances It may follow polycythaemia The disease is very similar to aleukaemic myeloid leukaemia In both there may be low or slightly raised leucocyte counts with many myelocytes or myeloblasts anaemia with normoblasts in the peri pheral blood and an enormous spleen It has been suggested that myelosclerosis is in fact a form of leukaemia in which the proliferating elements in the marrow have differentiated to produce fibroblasts as well as myeloid cells Whether or not this theory is accepted patients with myelosclerosis may sur vive longer than those with chronic leukaemia The presenting symptom may be pain in the enlarged spleen The diagnosis is suggested by the failure to aspirate marrow on marrow puncture and is made by histological demonstration of fibrosis in material from sternal trephine or rib biopsy Certain cases are now considered to be benefited by splenectomy or irradiation to the spleen though it used to be thought that splenectomy was inevitably fatal by removing the source of blood formation Otherwise the only treatment is periodical transfusion

Polycythaemia

An excess of erythrocytes in the blood is known as polycythaemia rubra usually shortened to poly cythaemia There are two main types secondary polycythaemia or erythrocytosis and the idiopathic variety or polycythaemia rubra vera

Erythrocytosis

This occurs in individuals as a response to lack of oxygen in the tissues One of the most important causes is residence at high altitudes when the

haemoglobin in men may rise to 18·0 g/100 ml with a corresponding rise in the erythrocyte count. This is one of the factors in altitude acclimatization and is entirely physiological Erythrocytosis may occur in advanced cardiac and pulmonary disease particularly in cases of congenital heart disease in which there is an admixture of arterial and venous blood There is no treatment for erythrocytosis its presence being beneficial at the time for that particular individual

Polycythaemia Rubra Vera

This is a relatively rare condition being distinctly less common than chronic myeloid leukaemia It is more common in males and usually manifests itself between the ages of 35 and 65 Some cases are familial. The marrow is hyperplastic throughout its extent, and the leucoblastic tissue and megakaryocytes are affected as well as the erythroblasts The total blood volume is increased and all vessels engorged with blood the spleen being particularly affected

Clinical Picture The patient usually complains of headache which is worse when lying down or a sense of fullness in the head Sometimes there is vertigo ringing in the ears or visual disturbances such as spots in front of the eyes There may be left upper abdominal pain from perisplenitis and neurological disorders such as paraesthesiae or even transient paralyses On examination the face shows a markedly congested appearance usually with some cyanosis in contrast the trunk is normal in colour The spleen is nearly always enlarged and may reach to the umbilicus A few cases that are associated with hypertension and have no splenomegaly have been referred to as polycythaemia hypertonica or Gaisbock s disease The cyanosis occurs because it reflects the absolute amount of reduced haemoglobin present, which is increased when the erythrocyte count is raised irrespective of the efficiency of oxygenation

Blood Picture The erythrocyte count is increased usually to 7–12 million cells/mm^3 The haemoglobin is raised to a lesser extent as the cells are somewhat microcytic There is commonly a polymorphonuclear leucocytosis of up to 40 000 cells/mm^3 and the platelet count may exceed a million Normoblasts may be found in the peripheral blood and there may be a reticulocytosis of about 5 per cent. The erythrocytes show varying degrees of anisocytosis and microcytosis

Diagnosis. This is easy in a patient with a plethoric countenance and splenomegaly but it may be difficult in the absence of the latter to distinguish early polycythaemia from a high normal count In polycythaemia however unlike even erythrocytosis the leucocytes and platelets are also increased and the erythrocytes may show morphological abnormalities

Course and Complications. The disease persists for life although patients may live a normal span Without treatment however they are likely to succumb to one of the following complications Thromboses due both to the plethora and the thrombocythaemia are extremely common cerebral thrombosis coronary thrombosis and mesenteric thrombosis may occur while polycythaemia vera is one of the commonest causes of hepatic vein thrombosis (Chiari s syndrome) Haemorrhages such as epistaxis and cerebral haemorrhage are not uncommon and there is an increased liability to gout and peptic ulcer In some cases myeloid leukaemia supervenes and in others myelosclerosis

Treatment Venesection may be effective in many instances for a considerable time One or two pints of blood are removed at intervals of six to eight weeks This often results in greater subjective improvement than the blood count would suggest Venesection may become ineffective by causing an iron deficiency state with an unchanged circulating cell-count, and it does not reduce the platelet count to any extent Radioactive phosphorus ^{32}P has a half life of 14 3 days and after intravenous injection it is almost entirely adsorbed by the bones thus irradiating the marrow After a single injection of 5–7 millicuries a remission may be induced lasting from two to five years If after eight weeks the erythrocytes still exceed six million the same dose or a little less may be repeated

Erythaemic Myelosis (Di Guglielmo s Disease)

If it is assumed that polycythaemia vera is the erythrocytic counterpart of chronic leukaemia erythraemic myelosis is analogous to acute leukaemia It is a very rare disease characterized by a fairly rapid fatal course with profound anaemia and an enlarged liver and spleen The blood shows numerous normoblasts far in excess of the reticulocytes present. A similar excess of normoblasts is found in the marrow and there is a reduction in the leucocytes and platelets The treatment consisting of blood transfusion is purely palliative A proportion of such cases terminate as acute myeloblastic leukaemia when they are known as erythroleukaemia

Haemorrhagic Thrombocythaemia

Another rare disease manifested by persistent increased platelet count of from one to three million/mm^3 The erythrocytes and leucocytes are unaffected The symptoms surprisingly are those of purpura not thromboses It is thought that ^{32}P may be effective

Leukaemia

In leukaemia there is an abnormal proliferation of leucopoietic tissue in the bone marrow and the deposition of similar tissue in other organs Usually there is a gross increase in circulating leucocytes but in certain cases known as aleukaemic leukaemia the total leucocyte count is not increased although immature cells may be found Leukaemia is best considered to be a neoplastic process as the overgrowth of the leucopoietic tissue is in many ways similar to that of carcinoma cells and actual tumours may occur It differs from most malignant processes first because it starts not as a circumscribed tumour but simultaneously throughout the bone marrow and secondly because many of the later deposits such as those in the liver are limited to certain parts of the organ and do not show true neoplastic invasion Experimentally leukaemias in fowls have been transmitted by cell free filtrates and in inbred mice by injections of blood from leukaemic mice These results are similar to those of tumour transmission experiments and neither tumours nor leukaemia have ever been accidentally transmitted from man to man The majority of cases occur spontaneously but there is a slight hereditary tendency and the incidence is somewhat greater in persons exposed to irradiation Leukaemia is certainly more common than early in the century Part of the increase in the number of cases recognized can be attributed to improved diagnosis but it is also possible that the incidence has increased owing to the widespread use of X rays The incidence is of much the same order as that of pernicious anaemia each general practitioner sees a new case every three to eight years The acute and chronic forms of the disease are about equally common

Acute Leukaemia

According to the type of cell affected acute leukaemia is divided into the lymphoblastic myeloblastic and monocytic varieties This differentiation is impossible on clinical grounds and depends on accurate identification of the primitive leucocytes In many cases the primitive leucocytes can be classified only tentatively and it is then best to make a diagnosis of acute leukaemia of type unspecified unfortunately the Registrar General demands the cell type for statistical purposes. The disease occurs at all ages and the lymphoblastic type is most common in children The pathology is similar to that of chronic leukaemia but the cell type is more primitive

Clinical Picture. The onset may be acute or insidious The cardinal features are fever haemorrhages ulceration of the mouth and fauces bony pains and anaemia The fever is very variable The haemorrhages are of the type found in thrombocytopenia Skin petechiae superficial bruising and oozing from mucous membranes particularly the gums are typically seen Retinal haemorrhages abnormal uterine haemorrhages and even cerebral haemorrhage also occur Ulceration of the fauces is possibly due to lack of adult functioning polymorphonuclear leucocytes similar ulceration occurs in agranulocytosis Pain in the bones may be demonstrated by tenderness over the sternum in children this may simulate acute rheumatism Even if fever is not pronounced the patient is markedly prostrated and ill looking The spleen liver and lymph glands particularly the cervical may be enlarged In monocytic leukaemia especially plaques infiltrated with leukaemic cells may occur in the skin Leukaemic deposits in various internal organs may in individual cases give rise to bizarre symptomatology

Blood Changes Anaemia is almost invariable even at the outset and is always a marked feature later It may be normocytic or macrocytic and circulating normoblasts are found particularly in myeloblastic leukaemia The platelets are usually grossly reduced although their absence does not seem to be the sole cause of the haemorrhages The leucocytes may be increased up to but rarely above 100 000/mm^3 and counts of about 20 000 are common In many cases the total white cells are less than 10 000 and may be very low though the normal circulating leucocytes are then largely replaced by myeloblasts lymphoblasts or monoblasts

Diagnosis and Course In many cases the clinical findings and blood count are incontrovertible but when the blood picture is less definite marrow puncture reveals masses of primitive cells and reduced numbers of erythroblasts and megakaryocytes In some cases of myeloblastic leukaemia the erythroblasts have a peculiar reticulation in their nuclei so that they resemble megaloblasts The clinical picture of agranulocytosis may be similar to that of acute leukaemia but there is no anaemia and primitive leucocytes are not present in the peripheral blood In glandular fever there may be faucial ulceration but the patient does not seem very ill and there is no anaemia although occasionally thrombocytopenia occurs diagnosis is made by the Paul Bunnell Test and marrow puncture Acute leukaemia may prove fatal in a few days but some cases survive for months Temporary remissions lasting a few months or so may occur spontaneously particularly in children

Treatment There is no cure for the disease and the only claim to be made of treatment is that it produces more remissions than occur spontaneously Such remissions can be induced far more frequently in children than adults Before embarking on a course of treatment it is wise to consider whether it is in the patient s best interests to prolong his suffering from a disease which if not acutely painful causes considerable discomfort Moreover many of the remedies have ill effects and, in particular repeated transfusion may be distinctly unpleasant especially for small children

Blood transfusion is the basis of any treatment it may be repeated and may of itself induce a remission Lymphoblastic leukaemia is the most likely variety to respond to steroids In adults 200–300 mg of cortisone a day is given initially and the dose is gradually reduced after a week For the myeloblastic variety 6-mercaptopurine orally in a dose of 2 5 mg/kg of body weight is sometimes effective but improvement does not start for two or three weeks it is of less use in lymphoblastic leukaemia but will occasionally induce remissions in monocytic leukaemia Folic acid antagonists such as aminopterin induce remissions in children but are toxic producing particularly ulceronecrotic lesions of the gastro intestinal tract. Irradiation busulphan and nitrogen mustards are ineffective in acute leukaemia Symptomatic treatment in cases with stomatitis should include antibiotics if it is hoped to secure a remission

Chronic Leukaemia

The majority of cases of leukaemia can be easily separated into acute or chronic varieties but occasional subacute types occur Chronic leukaemias can with certainty be subdivided into myeloid lymphatic and the rare eosinophilic leukaemia on the basis of their blood changes but clinically the difference may be slight. There is no true chronic variety of monocytic leukaemia Eosinophilic leukaemia on the other hand is invariably chronic but of such rarity as not to merit further discussion

Pathology Hyperplastic greyish bone marrow is found throughout the skeleton including the long bones The predominant cells are either small lymphocytes with occasional lymphoblasts or myelocytes with some myeloblasts The spleen is uniformly enlarged and the site of infarcts and perisplenitis microscopically the Malphigian corpuscles have disappeared and the organ appears a mass of myelocytes or lymphocytes A similar appearance is found in the lymph glands and in myeloid leukaemia the myelocytes first appear in the medulla and compress the follicles The spleen is chiefly affected in myeloid leukaemia however and the glands in lymphatic leukaemia The liver shows infiltration which is confined to the portal spaces in lymphatic leukaemia but is diffuse throughout the organ in myeloid leukaemia Collections of leukaemic cells known as leukaemic deposits may occur in any organ but are most noticeable in the skin

Clinical Picture Chronic leukaemia occurs equally in both sexes usually after the age of 35 unlike the acute form it is distinctly uncommon in children The onset is insidious and the patient may complain of tiredness weakness or loss of weight, the latter being due perhaps to the increased basal metabolic rate which accompanies the vast cellular proliferation Alternatively the presenting symptom may be painless glandular enlargement in the lymphatic form or in the myeloid form gross splenomegaly which may extend to the right iliac fossa and give rise to a dragging sensation Especially in lymphatic leukaemia plaques in the dermis pruritus or a generalized erythema may be the first manifestation of the disease Pain in the bones and joints may also occur and pain may be elicited on percussing the sternum Priapism is an occasional manifestation of myeloid leukaemia Lymphatic leukaemia may present as Mickulicz s syndrome or mediastinal obstruction In women infiltration of the reproductive system may cause amenorrhoea and loss of fertility but if pregnancy does occur a healthy child is usually born although the disease may be aggravated As the disease progresses there may be cachexia and as a result of the anaemia cardiac decompensation with such manifestations as dyspnoea oedema and effusions into the serous cavities Haemorrhages which usually occur late include skin petechiae bruising retinal haemorrhages and cerebral haemorrhage which may be the immediate cause of death

Blood Changes. Anaemia is usually present and is of normocytic type though occasionally macrocytic Erythroblasts may be present, particularly in myeloid leukaemia The platelets are usually decreased but may be increased initially in the myeloid form The leucocytes in chronic lymphatic leukaemia usually number 60 000–200 000/mm³ but the figures may be outside these limits in either direction Almost all the cells are small lymphocytes with very occasional lymphoblasts the absolute numbers of the polymorphs are not increased In lymphatic leukaemia there is not uncommonly an associated autoimmune haemolytic anaemia In myeloid leukaemia the total leucocyte count is typically higher ranging from 100 000 to 400 000/mm³ or more Most of the cells are mature polymorphs but some 15–50 per cent are myelocytes Mature

eosinophil and basophil leucocytes are also commonly increased while myeloblasts are scanty

Diagnosis and Course Blood pictures similar to that of myeloid leukaemia may occur in the course of certain infections particularly tuberculosis and are known as leukaemoid reactions Typically the counts are lower and fewer myelocytes are present but if confusion arises it may be settled by marrow puncture when myeloblasts are found in larger numbers in leukaemia than in a leukaemoid state In very rare extreme examples the finding of leukaemic infiltrations post mortem may be the sole means of reaching a diagnosis As a rule the clinical findings and blood count are quite sufficient for arriving at a decision The high lymphocytosis of whooping cough is easily distinguished on clinical grounds Metabolic oddities which accompany leukaemia such as increased blood uric acid and raised basal metabolic rate are not of diagnostic value Although spontaneous remissions occur, the disease is invariably fatal usually in three to five years occasional cases may survive for ten years Immediate causes of death include intercurrent infections intractable anaemia haemorrhage into an essential organ or an acute leukaemic termination with myeloblasts or lymphoblasts The onset of haemorrhages increasing anaemia or the appearance of primitive leucocytes suggests an early demise

Treatment There is no evidence that any form of treatment prolongs life all that can be expected is to increase the remission rate and enable the patient to live as comfortable a life as possible Remedies should not be pressed to the point of toxicity The standard therapy is irradiation by deep X rays which is given in the first instance to the spleen if enlarged and later to the skeleton If successful the leucocyte count falls almost to normal and the haemoglobin rises Such a remission may last for a year but repeat courses are less effective and usually not more than three can be given Radioactive phosphorus is not to be preferred to conventional radiotherapy Nitrogen mustards although less effective than irradiation can be used as an alternative but they produce nausea vomiting and vertigo which can to some extent be prevented by dramamine 100 mg immediately after the injection The bis nitrogen mustard is the best and 0 1 mg/kg can be given intravenously on alternate days for up to seven injections Careful blood counts are required to prevent excessive destruction of haemopoietic tissue Triethylenemelamine (TEM) can be given orally or intravenously and is less toxic than nitrogen mustard The intravenous course consists of five injections of 2 mg spread over a month th oral course of 2 5–5 mg before breakfast twice or three times a week until 20–30 mg have been given Chlorambucil is chemically related to the nitrogen mustards and is effective orally in chronic lymphatic leukaemia The dose is 0 2 mg/kg of body weight per day for a course of 3–6 weeks. Busulphan given orally in a dose of 0 06 mg/kg daily may be effective in cases of chronic myeloid leukaemia Lymphatic leukaemia complicated by haemolytic anaemia responds temporarily to steroids Apart from drug therapy blood transfusion may be given to those cases with a severe anaemia which does not improve as the leukaemic process abates

Aleukaemic Leukaemia

In about one in five cases of leukaemia both acute and chronic there is no substantial increase in the total circulating leucocytes The acute form hardly differs from the classical acute leukaemias as those cells that are present are primitive Chronic aleukaemic leukaemia in the main is similar to its fully leukaemic counterpart but requires separate consideration in some respects Many cases have splenomegaly or lymphadenopathy but some present as an intractable anaemia without significant physical signs Variable numbers of primitive leucocytes and erythroblasts may be present in the blood but marrow puncture is necessary to distinguish aleukaemic leukaemia from such diseases as pernicious anaemia aplastic anaemia and myelosclerosis Cases may be aleukaemic throughout their course aleukaemic cases may later become frankly leukaemic or the reverse may occur The treatment of chronic aleukaemic leukaemia has often to be restricted to blood transfusion as the low leucocyte count does not allow a large margin for other forms of therapy

Chloroma

This is a rare type of acute myeloblastic leukaemia occurring in children and adolescents In addition to the usual features of acute leukaemia there are one or more tumours These are often subperiosteal especially around the skull but they also arise in other organs The tumours may precede the blood changes and when cut into show a peculiar greenish colour microscopically they are composed of myeloblasts

Lymphomata (Malignant Reticuloses)

The principal cells in lymph glands are lymphocytes and reticulum cells from both of which tumours may arise From lymphocytes arise lymphosarcoma and the more benign giant follicular lymphoblastoma in which the tumour cells are confined to the follicles instead of diffusely infiltrating the gland Diffuse lymphosarcoma however not infrequently supervenes on the follicular variety From reticulum cells arise the comparatively benign reticular lymphoma (Hodgkin s paragranuloma) in which reticulum cells including Sternberg Reed giant cells are surrounded by lymphocytes so as to resemble bird s eyes and the more rapidly progressive Hodgkin s disease (lymphadenoma) in which there is more marked reticulum cell proliferation eosinophil infiltration and a variable degree of fibrosis There is now little doubt that Hodgkin s disease should be regarded as a neoplasm but in the past various other theories as to its aetiology were popular the chief was that it was a virus disease or an infective granuloma allied to tuberculosis Still more undifferentiated tumours of lymph glands are the reticulum cell sarcomata

The lymphomata differ among themselves clinically in minor particulars The more benign types may run a courses of 15 to 20 years the more malignant may be fatal in a few months They occur at all ages but are rare in early childhood In addition to lymphatic glands spleen liver alimentary tract and bone may be affected Giant follicular lymphoblastoma has a predeliction for producing pleural effusions and occurs comparatively late in life Hodgkin s disease may be associated with erythrodermia and show discrete foci of infiltration in bone marrow or spleen the so called hard bake spleen Reticular lymphoma usually presents with affection of a single group of glands most often cervical Lymphosarcomata in a minority of cases are accompanied at some stage by the blood changes of lymphatic leukaemia In other respects the clinical manifestations of the lymphomata are so similar that they can only be differentiated histologically

Clinical Picture The presenting feature of the lymphomata is often the discrete usually painless enlargement of a solitary lymph gland or more commonly group of glands such as the supraclavicular In such cases there may be initially no other symptoms though if the enlarged glands give rise to pressure as when the mediastinum is involved there may be cough dyspnoea and even pulmonary collapse or pleural effusion The glands may attain a size of up to about 3 in in diameter are of a rubbery consistency and remain discrete and mobile until late Other cases present as a generalized glandular enlargement with or without splenomegaly and hepatomegaly usually accompanied by a feeling of weakness and sometimes by fever When the affected glands are deep seated and cannot be palpated an obscure febrile disorder may be the first manifestation Period s of a week s fever separated by slightly longer afebrile periods (the Pel Epstein fever) are usually associated with Hodgkin s disease Lymphosarcomata in particular may present as visceral tumours which can be differentiated from carcinomata only histologically Initially there is no anaemia In Hodgkin s disease there is an inconstant slight eosinophilia though this is of little diagnostic import. Spontaneous or induced remissions may occur in which the tumour masses disappear but as the disease progresses the patient eventually becomes profoundly anaemic and cachectic and further treatment becomes ineffective

Diagnosis. Clinically simple inflammatory glandular enlargement may often be distinguished by the smaller size of the glands the presence of a primary inflammatory lesion pain and more rapid onset Tuberculous glands in the neck affect the tonsillar glands rather than the supra clavicular and are matted together at an early stage A definite diagnosis can often be made by histological examination of an excised gland though in many cases the histology is at first inconclusive and a further gland may have to be sectioned

Treatment. This is palliative although initially masses of glands may regress with great rapidity Discrete masses of glands should be removed surgically and very occasionally this is not followed by recurrence In general however treatment is similar to that of chronic lymphatic leukaemia Radiotherapy is the most generally used method chlorambucil TEM and nitrogen mustards are also of considerable value either initially or if the disease becomes refractory to radiotherapy

Myelomatosis

The essential lesion of this disease is an excessive proliferation of plasma cells in diffuse or circumscribed deposits in the bone marrow It is best considered to be a neoplasm It affects both sexes equally is almost entirely confined to the elderly and is relatively uncommon but not as rare as thought formerly A few plasma cells are normally present in the bone marrow They are a source of

circulating globulin and if this is increased the plasma cells are always slightly increased as well Myelomatosis cannot accurately be regarded as a leukaemia affecting plasma cells as there are a large number of circulating plasma cells in the blood only very rarely and the deposits in the marrow are often discrete resembling secondary deposits of carcinoma In a few cases extramedullary tumours are found and occasionally the disease presents as a solitary plasmacytoma of bone

Clinical Picture The onset is insidious with pain in the bones particularly backache the most prominent complaint There may be tenderness to pressure over the bones skeletal deformities such as kyphosis or pathological fractures or paraplegia from pressure of myelomatous deposits on the spinal cord Other cases may present as unexplained anaemias or incipient uraemia occasionally there are haemorrhagic manifestations The symptomotology is often very vague due partly to concomitant nitrogen retention and partly to the advanced age of the patient

Investigations There is usually anaemia which may be of simple normocytic or macrocytic type but may be leuco erythroblastic with a few primitive leucocytes and erythroblasts A very few cases show a leukaemia blood picture with circulating plasma cells The majority of cases show hyperglobulinaemia the total plasma protein being as high as 20 g/100 ml the greater part of which is abnormal globulin usually γ but sometimes β globulin This of itself may cause auto agglutination of erythrocytes *in vitro* a great increase in the sedimentation rate and a haemorrhagic tendency Many cases have Bence Jones proteose in the urine which is identified by its property of coagulating at a lower temperature than the usual urinary proteins and redissolving at 100 C. Even in the absence of Bence Jones proteinuria there may be nitrogen retention due to an associated nephritis If there is gross hyperproteinaemia the non ionized fraction of the serum calcium is also increased Multiple punched out areas in the bones can sometimes be demonstrated radiologically Serum alkaline phosphatase is normal or slightly increased The diagnosis depends on finding gross excess of abnormal plasma cells on marrow puncture but this may have to be repeated when the deposits are localized Electrophoresis of serum proteins when the plasma globulin is raised may give an almost diagnostic picture

Treatment If untreated the disease is steadily progressive and death results from uraemia or intercurrent infection No treatment is very effective in slowing up the process or relieving pain Urethane in doses of 1 5–3 g a day is of some use Stilbamidine 50 mg intravenously followed by 100 mg and later 150 mg at two to four day intervals for a total of 15–20 injections has some effect but is toxic Radiotherapy is of little value

Enterogenous Cyanosis

Methaemoglobinaemia and Sulphaemoglobinaemia

In these conditions there is cyanosis unaccompanied by dyspnoea or polycythaemia but with some degree of weakness and often intolerable headache They are not dangerous They are commonly caused by drugs especially the sulphonamides but also by phenacetin sulphonal potassium chlorate and aniline derivatives Each drug may cause either methaemoglobinaemia or sulphaemoglobinaemia by a mechanism which is obscure Water containing more than 10–20 parts/million of nitrates may cause methaemoglobinaemia in infants The diagnosis depends on the spectroscopic demonstration of the appropriate haemoglobin derivative inside the patient s erythrocytes There is no anaemia

Treatment consists in withdrawal of the drug Methaemoglobinaemia usually clears up rapidly in a day or two sulphaemoglobinaemia may persist for weeks Temporary improvement can be brought about by methylene blue (0 1 to 0 2 ml/kg body weight of a 1 per cent aqueous solution intravenously or 0 5–1 0 g orally per day) or ascorbic acid in doses of 200–500 mg by mouth daily

Familial methaemoglobinaemia is a rare condition in which cyanosis is present from birth It is apparently due to diminished coenzyme factor I activity leading to displacement of the equilibrium Hb$\rightleftharpoons$MHb The shed blood returns to normal only on treatment with methylene blue whereas drug induced methaemoglobinaemia disappears slowly on exposure to the atmosphere

Glandular Fever (Infectious Mononucleosis)

A benign infectious disease typified by fever enlarged lymph glands and characteristic blood changes

Aetiology and Pathology It is now considered to be a virus disease although no specific agent has been isolated The infectivity is low the vast majority of cases occur sporadically but epidemics have been encountered In the few cases studied at

autopsy the pathological changes are confined to focal proliferation of atypical mononuclear cells although jaundiced cases may have focal acute hepatitis. In general the disease is self limiting and non fatal.

Clinical Picture The vast majority of persons affected are between 16 and 30 so that it is characteristically a disease of students It is less common in children in whom pyrexia in association with enlarged lymphatic glands in the neck from other causes so often occurs Several clinical types have been described of which the most important are the glandular and the anginose The glandular type starts with fever up to 102 -103 F and malaise followed by glandular enlargement at variable intervals The enlargement may be inconspicuous or obvious and tender Usually the neck glands are principally involved but in a proportion of cases there is generalized glandular involvement and slight splenomegaly In a few cases a rubelliform rash appears between the fourth and tenth day The illness usually lasts for 10 to 14 days after which the pyrexia subsides but convalescence may be protracted and relapses may occur In the anginose type the predominant feature is a sore throat with membrane formation resembling diphtheria Glandular fever may also present as jaundice very similar to infective hepatitis or with encephalitic or polyneuritic symptoms

Blood Changes. Characteristically atypical mononuclear cells which in part resemble lymphocytes and in part monocytes are present. They are about the size of monocytes with rather bluish grey abundant cytoplasm that may contain azure granules or be fenestrated The nucleus is oval or slightly indented and has no nucleoli The total leucocyte count may be normal or increased but the neutrophils are reduced These changes may not take place for some days and in the initial stages there may be a neutrophil leucocytosis There is no anaemia and no specific bone marrow changes Symptomatic thrombocytopenic purpura is a rare concomitant. At about the same time as the blood picture appears but sometimes later the Paul Bunnell test becomes positive This test, called after its two discoverers consists in the demonstration of agglutinins for sheep s erythrocytes in the patient s serum The interpretation of the test varies with the exact method employed but apart from glandular fever there may be a low titred agglutinin for sheep s erythrocytes in the serum of normal persons and a higher titred agglutinin may develop in cases of serum sickness Glandular fever agglutinins may be absorbed by ox erythrocytes but not by guinea pig kidney Normal agglutinins are absorbed by guinea pig kidney but not by ox cells serum sickness agglutinins are absorbed by both False positive Wasserman reactions are common

Diagnosis For unequivocal diagnosis both the typical blood picture and a positive Paul Bunnell should be present, although the latter may have to be repeated before becoming positive Cases are comparatively common in which the blood picture is typical, but the Paul Bunnell remains negative throughout. Minor alterations in the blood picture alone provide insufficient grounds for diagnosing glandular fever as small numbers of atypical mononuclears may be found in other conditions such as infective hepatitis and the acute exanthemata Cases in which there are no serological or cellular changes may possibly exist but the matter at the moment is incapable of proof The clinical picture may be similar in infective conditions of the upper respiratory tract and in acquired toxoplasmosis Generalized glandular enlargement accompanied by splenomegaly is more likely to be glandular fever than enlargement of the cervical glands alone Acute leukaemia may resemble glandular fever but the patient is obviously more ill anaemia is almost invariable and the other blood changes usually make distinction easy Diagnosis of the anginose type is almost always made after an ulcerated throat present for a week has failed to respond to antibiotics and is accompanied by a temperature rather out of proportion to the disability It is quite common for throat swabs to yield growths of *Staph aureus* or coliform bacilli A similar clinical picture occurring in angranulocytosis is readily distinguished by the blood picture

Treatment There is no specific treatment. During the acute stages the patient is more comfortable in bed and antibiotics may be required for secondary throat infection Contacts should not be placed in quarantine

CHAPTER 20

Rheumatic and Collagen Disorders

JOHN W TODD

THE so called rheumatic disorders are a group of ill understood conditions affecting the joints and soft tissues Our ignorance of their aetiology is pro found Apart from trauma in a few circumstances very few agents such as bacteria which are the direct cause of pathological changes have been identified and there is little evidence to incriminate such factors as strain emotion and fatigue A good deal is known about the pathology of some varieties of these disorders—for example of osteoarthritis and rheumatoid arthritis —but the pathology of many others especially when the soft tissues are the main seat of the trouble remains obscure (though imaginative pathology has given rise to such con ditions as fibrositis and sacro iliac strain ')

Sometimes patients cannot even be fitted into a definite clinical syndrome Thus although many patients clearly have rheumatoid arthritis osteo arthritis or rheumatic fever others have some features suggesting rheumatic fever and some sug gesting rheumatoid arthritis or some suggesting rheumatoid arthritis and some suggesting osteo arthritis A few patients who for a year or two seem to have rheumatoid arthritis may then develop the manifestations of systemic lupus erythematosus Among the subjects of non articular rheumatism" there may be such a bewildering variety of features as to make classification difficult or impossible

Recently the term collagen disease has become increasingly popular It was first introduced in 1942 and was applied to systemic lupus erythematosus and generalized scleroderma It is now often applied to some of the rheumatic disorders and other con ditions of obscure aetiology in which the main pathological changes are in the connective tissues and the most characteristic lesion is fibrinoid necrosis Among the disorders placed in this cate gory are rheumatoid arthritis ankylosing spondy litis rheumatic fever systemic lupus erythematosus polyarteritis nodosa dermatomyositis scleroderma and Henoch Schonlein purpura Glomerulo neph ritis malignant hypertension erythema nodosum erythema multiforme pemphigus ulcerative colitis serum sickness and many others are also sometimes included There is indeed a tendency to describe any ill understood chronic or sub acute disorder as a collagen disease How much this concept has im proved our understanding of these obscure condi tions is questionable but the term is now widely used and as long as our understanding of them remains so meagre the category of collagen dis eases is perhaps a useful one

Scleroderma and pemphigus are usually said to be dermatological conditions and will not be dealt with in this book Henoch Schönlein purpura is considered under disorders of the blood (p 493) ulcerative colitis under the alimentary tract (p 196) malignant hypertension and polyarteritis nodosa under the cardiovascular system (pp 257 and 295) and glomerulo nephritis under the renal tract (p 472) The more important of the remainder will be considered in this chapter

Psychiatric Aspects. Many patients complain of pain in the limbs neck or back which is of psycho logical origin but is described by them as rheuma tism Psychogenic rheumatism is indeed a commonly used expression The manner by which pain of this kind can be differentiated from that due to local lesions was discussed on p 12. But in interpreting this pain mistakes are easily made and it is often attributed wrongly to an organic process If it is recognized that the emotions are responsible for the pain it is still possible to reach a wrong diagnosis by hypothesizing the psycho somatic disease fibrositis which is the supposed immediate cause of the pain In common with other conditions of obscure aetiology even those rheu matic disorders with undoubted pathological changes such as rheumatoid arthritis are now also said at least in some cases to be psychosomatic Although it is possible that individual attacks are precipitated by psychological factors there is no good evidence that such factors are usually import ant in the aetiology either of rheumatoid arthritis or of other rheumatic disorders

In practice the important psychiatric aspects of the rheumatic disorders are in their effect on the emotions and in the attitude which patients have towards them Many of these disorders are chronic painful and disabling and their victims are apt to

become depressed to give way to self pity and to make no attempt to overcome them The difference in disability between two people with rheumatoid arthritis whose joints are apparently similar is often striking There may be a similar difference in the amount of pain of which they complain There is little doubt too that the doctor can often do some thing and can sometimes do much in encouraging people to overcome their disability

Investigations. Special methods of investigation play only a small part in most cases There are very few procedures which are in any sense diagnostic and the main value of investigations is in the dis covery of such comparatively rare conditions as collapsed vertebrae or myelomatosis which cause pain and other symptoms superficially suggesting a rheumatic disorder Indeed in so far as these dis orders are susceptible of precise diagnosis they are as a *rule essentially clinical syndromes There are* it is true fairly characteristic X ray changes of rheumatoid arthritis but these are not seen in the early stages and the clinical picture is much more characteristic Osteo arthritis gives rise to early and more definite X ray changes which may long pre cede the symptoms But the important means of assessing the picture is the pain and stiffness of the joints it is a matter of indifference to a patient that he has radiological changes of osteo arthritis if he can move his joints fully without pain

Next to X rays perhaps the most widely used investigation is the erythrocyte sedimentation rate (E S R) This is always more or less raised in rheumatic fever rheumatoid arthritis and ankylos ing spondylitis though is rarely raised in osteo arthritis and most types of non articular rheuma tism In general the more severe are the joint changes and the constitutional disturbance and the higher the fever of rheumatic fever and rheumatoid arthritis the higher is the E S R But the clinical picture is sufficient testimony of the severity of the process and it is questionable whether the E S R gives further useful information On the other hand patients with pain and malaise but lacking other evidence of rheumatic disorder may sometimes be found to have a high E S R this should suggest that some such condition as secondary deposits in bone may be present

Cases of rheumatic fever active rheumatoid arthritis or ankylosing spondylitis commonly have normochromatic anaemia the severity of which also corresponds as a rule to the severity of the clinical picture

Certain special methods of investigation may nevertheless reveal virtually diagnostic features of some of the rarer collagen diseases The L E cell strongly suggests systemic lupus erythematosus the histological appearances of polyarteritis nodosa are characteristic and advanced cases of dermatomyo sitis may show fairly characteristic histological changes in biopsies of muscle

Treatment In general this is unsatisfactory A vast number of remedies has been used and that in itself suggests that none is highly successful There is no specific cure for any of these disorders As a rule the most consistently successful remedies are the analgesic drugs especially the salicylates Sometimes notably in rheumatic fever the salicy lates apparently do more than relieve pain they are also antipyretic and may have some effect on the disease process Various types of physiotherapy are employed on an enormous scale but their value is unproven Cortisone and the other steroid drugs have been widely used in recent years and although they may give dramatic benefit in the short run *their long term effects have been disappointing* Their most certain value seems to be in suppressing the manifestations of systemic lupus erythematosus polyarteritis nodosa and acute dermatomyositis Radiotherapy seems to relieve the subjects of ankylosing spondylitis but in other circumstances has little value Other remedies which are useful sometimes are splintage to immobilize joints or pre vent contractures remedial exercises and in a few special situations certain orthopaedic operations

Rheumatic Fever (Acute Rheumatism)

There is a fairly well defined syndrome of rheu matic fever with fever painful and swollen joints which later recover completely and a liability to carditis But there are many border line cases with minor symptoms and a few border line cases of a more chronic nature approaching the picture of rheumatoid arthritis and it is impossible to draw a line clearly marking off rheumatic fever from other conditions Moreover nearly half those with rheumatic heart disease give no history of rheumatic fever

Rheumatic fever can occur at any age though it particularly affects children and young adults and is rare in infants and the very old It occurs in all parts of the world but is most common in the temperate countries Its incidence among the poor is much higher than among the rich In the last few decades there has been a great fall in its incidence Before the Second World War a high proportion of the children and young adults in the medical wards of hospitals had rheumatic fever now such cases are fairly rare

Aetiology There can be no doubt of the associa tion between the disease and infection by *group A* haemolytic streptococci The main fields of con troversy have been about the nature of the re

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subsides Leucocytosis is usual but of little or no practical importance Electrocardiographic changes including a prolongation of the P R interval occur sometimes though they are of little prognostic significance The X ray may show cardiac enlargement but the prognostic significance of this finding is also uncertain

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A few quite independent disease processes may superficially simulate rheumatic fever Osteomyelitis causes severe limb pain but the process is confined to one part there is tenderness over an epiphysis rather than over the joint the fever is usually higher and there is marked leucocytosis Gout causes painful red and swollen joints but the previous history usually gives the clue the big toe joints are particularly affected and middle aged men are the chief victims The response to salicylates is sometimes a useful therapeutic aid to diagnosis If there is no quick improvement, some other cause than rheumatic fever for pain and tenderness should be sought

Course and Prognosis. In practice the course of rheumatic fever is always affected by salicylate or other treatment Untreated the disease probably subsides after some weeks or months The prognosis of the individual attack is good and very few patients die in the acute stage with fulminating symptoms and hyperpyrexia or heart failure Recurrences are common and each increases the liability to rheumatic heart disease This is the sole important sequel of rheumatic fever and many years may elapse before symptoms resulting from it develop

Prevention If infection by group A haemolytic streptococci could be prevented rheumatic fever would probably not occur With present knowledge the only way of doing this would be to administer sulphonamide penicillin or other antibiotic to the whole population continuously This is obviously not practicable and would probably do more harm in other ways than good in preventing rheumatism even if it were The efficient treatment by these drugs of group A haemolytic streptococcal infections as they arise would no doubt lessen the incidence of rheumatic fever though it would not prevent the many attacks due to subclinical streptococcal infections But clinically it is impossible to know whether such symptoms as sore throat are due to this organism To differentiate the infections due to this and to other organisms swabbing would be necessary—a formidable task To treat every case of sore throat with anti bacterial drugs would encourage the development and spread of resistant staphylococci and other organisms

In practice the legitimate field for prophylactic measures is among those who have already had one attack of the disease both because they are more liable to future attacks and because each attack increases the likelihood of permanent cardiac damage It has been shown that continuous penicillin will greatly diminish further attacks and sulphadiazine is probably nearly as effective The usual dose is 1 2 M units of benzathine penicillin by intramuscular injection once per month phenoxymethyl penicillin (Penicillin V) 125 mg twice daily by mouth or sulphadiazine 0 5 to 1 g daily depending on the patient s weight This should be continued at least for several years

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lationship between the streptococcal infection and the rheumatic manifestations and as to whether other organisms or other aetiological agents can sometimes be responsible for the disease But that the joint and cardiac manifestations are not directly due to haemolytic streptococci in these regions seems clear and blood cultures are sterile

Commonly some 2 to 3 weeks after an attack of scarlet fever tonsillitis or other upper respiratory infection due to haemolytic streptococci the rheumatic manifestations begin But only some 5 per cent of those who have such infections develop rheumatic fever and it seems that their tissues have an unusual sensitivity to the products of the organisms (A similar state of affairs arises in acute nephritis which also occurs some weeks after streptococcal infection) There is evidence for supposing that streptococcal allergens and toxins act synergistically upon mesenchymal cells to produce the rheumatic syndrome in susceptible persons No convincing evidence to incriminate other organisms has been advanced and in the light of present knowledge it seems reasonable to assume that the haemolytic streptococcus is invariably responsible The fact that it cannot always be isolated proves nothing because of the interval of weeks between the infection and the rheumatism it is always possible that a symptomless streptococcal infection caused the trouble but cleared up completely by the time the rheumatism developed

Whether other factors may contribute to the development of rheumatic fever is uncertain It is undoubtedly more common among poor and crowded town dwellers than among better off country people but the explanation may well be that streptococcal infection is much commoner among the former than among the latter Damp is widely believed to bring on the disease but even if this is true haemolytic streptococci may spread more freely in damp than in dry conditions There is little evidence for supposing that trauma—other than by causing an open wound which provides a breeding place for the organism—and emotional upsets may precipitate the disease There is sometimes a hereditary tendency which can be satisfactorily explained on the grounds that the unusual sensitivity to the products of haemolytic streptococci may be familial

Pathology The Aschoff body is the characteristic miscroscopic lesion In size it is about the limit of visibility It consists of a centre of necrotic material the Aschoff cells (which are large occasionally multi nuclear cells of the epitheloid type) lymphocytes plasma cells a few polymorphonuclear leucocytes and proliferating fibroblasts This lesion is most abundant in the myocardium chiefly around the arteries and is also found in other parts of the heart and in the synovial tissues The affected joints contain viscid synovial fluid and the periarticular tissues may be oedematous Affected heart valves are thickened with vegetations (which consist of fibrin and various blood cells) along their surface at the lines of contact of their cusps

Clinical Picture Sometimes without warning and sometimes a few weeks after a sore throat or other upper respiratory infection limb pains malaise sweating and fever begin The onset may be most insidious but is occasionally fairly sudden Frequently the pain flits from joint to joint and usually the larger joints are most affected The joints although tender and painful if moved often look normal although sometimes they are swollen and when the swelling develops the pain usually diminishes There is usually a variable fever in the region of 101 to 103 F Tachycardia may be out of proportion to the fever Sweating is frequently profuse and the sweat may have an unpleasant odour Occasionally there is a transient rash suggesting erythema multiforme Palpable rheumatic nodules usually painless are often found over bony prominences or on tendons especially in children

The most important feature of rheumatic fever is carditis Since this may occur without definite signs it is impossible to be sure whether or not it is an invariable accompaniment though many patients never show evidence of rheumatic heart disease in later years Moreover the interpretation of cardiac signs during the acute disease is difficult. Although marked tachycardia and mitral systolic murmurs are suggestive of cardiac involvement their precise significance is uncertain Diastolic murmurs a pericardial friction rub due to pericarditis or definite cardiac enlargement as shown by X ray are on the other hand convincing signs of cardiac involvement But the important cardiac damage is that leaving *permanent sequelae* the nature and gravity of these sequelae can only be assessed in subsequent years

Rare manifestations of rheumatic fever include pleurisy and pneumonia epistaxis and abdominal pain The immediate cause of the latter is uncertain but it may be due to panarteritis affecting the mesenteric vessels

Sydenham s chorea (p 445) is closely related to rheumatic fever and it may be followed by rheumatic heart disease though there is less likelihood of this than after rheumatic fever Attacks of chorea may alternate with attacks of rheumatic fever

Investigations The E S R is always raised during the active phase often above 100 mm after 1 hr (Westergren) Anaemia usually normochromic is nearly always present and disappears as the process

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advised efforts should be made to minimize his anxiety When finally allowed up he should be reassured informed that palpitation weakness and giddiness are not due to heart disease and there should not be repeated cardiac examinations With this reassurance he may avoid cardiac anxiety symptoms such symptoms dating from rheumatic fever which has apparently caused no organic damage are frequently seen

Painful joints should be protected from pressure and trauma by a cradle and perhaps by wrapping them in cotton wool There is no evidence that the common practice of applying ung meth sal or other substances to them has any good effect

Diet can safely be left to the patient s inclinations

An important question is whether the course of rheumatic fever is influenced by treatment to eradicate group A haemolytic streptococcal infection given after the rheumatic manifestations have developed Such treatment certainly has no dramatic effect and since the rheumatism follows some weeks after the infection which has then as a rule cleared up this is not surprising Only a controlled series could determine whether it has any effect but if the patient still has a sore throat or if a throat or nose swab grows the streptococci it seems reasonable to give a course of penicillin

A most important remedy for rheumatic fever is the salicylates About 8 g (120 gr) of sodium salicylate or aspirin should be given daily in divided dosage to a child of 12 until the fever and pains have been relieved when the dose should be gradually reduced to about half this amount This treatment is so successful that if the symptoms persist the diagnosis should be questioned Unfortunately salicylate does not prevent cardiac sequelae Whether it lessens them is uncertain and since it would be unjustifiable to conduct a clinical trial in which half the patients are given no salicylate this uncertainty is likely to persist

Salicylate treatment is usually continued at least until the sedimentation rate has been normal for a few weeks There is no evidence as to whether very prolonged salicylate treatment would give superior results but it seems possible that it might and it is unlikely to do harm If the treatment were continued indefinitely recrudescence of the joint symptoms and fever would without reasonable doubt be prevented though it does not necessarily follow that further cardiac damage would not occur There is moreover an alternative and probably superior method of preventing relapses—the continuous administration of penicillin or sulphonamide The influence of indefinite salicylate therapy would form a useful subject for a clinical trial

Steroid drugs will relieve the symptoms of rheumatic fever even more rapidly than does salicylate Whether the end results of steroid treatment are superior to those of salicylate treatment is at present uncertain but there is suggestive evidence that the patient is given the best chance of avoiding cardiac sequelae by a combination of both in high dosage The initial dose of cortisone should be about 300 mg daily falling to 50 mg daily after 6 weeks The salicylate dosage should be that given above This combination should probably be continued until the E S R has been normal for some weeks If steroids are not used initially patients who do not satisfactorily respond to salicylates should undoubtedly be given them

Rheumatoid Arthritis

Although the patients given this diagnosis differ very greatly rheumatoid arthritis is as a rule a definite and recognizable entity and is by far the most common form of polyarthritis It may develop at any age but usually between early adult life and middle age Women are affected more than men in the ratio of about 3½ to 1 Whether its incidence has changed in recent years is doubtful

Aetiology Very little is known about aetiology An attractive hypothesis is that the condition is due to an abnormal reaction to the products of some organism or other antigen (as rheumatic fever is due to group A haemolytic streptococci) since the fever and constitutional upset suggest an infection No such organism has been identified in spite of intense efforts

Numerous aetiological factors have been incriminated including emotional upsets focal sepsis damp housing conditions wet and cold weather endocrine disturbances and vitamin deficiencies There is no good evidence that any of them plays more than a very small part Occasionally the disease follows closely upon some grave psychological trauma but even if the relationship is causal not coincidental in these few cases there is no justification for concluding that the majority of cases of rheumatoid arthritis are psychosomatic There is little if any tendency for the disease to run in families Remissions often occur in pregnancy or after attacks of jaundice but this has shed no light on aetiology

Pathology Initially the synovial membrane becomes thickened and oedematous with increased vascularity Later the articular cartilage is encroached upon by the thickened synovial membrane and becomes eroded and osteoporosis of the nearby bone may follow Effusion is common The inflammatory process may be arrested at any stage and be followed by fibrosis leading to adhesions within and around the joints and consequent ankylosis In

advanced cases complete disorganization of joints particularly of the hands may occur Muscle atrophy of greater or less degree is invariable

Clinical Picture The onset is usually insidious Frequently there are prodromal symptoms such as malaise anorexia loss of weight and indefinite pains for some weeks or months before the joint symptoms begin In some two thirds of cases several joints are initially involved in the remaining third only one joint Occasionally the onset is acute and suggests rheumatic fever

All joints can be affected The most frequently involved are the metacarpo phalangeal joints the proximal interphalangeal joints of the fingers the wrists knees and metatarso phalangeal joints The distal interphalangeal joints of the fingers are rarely affected and the least frequently involved joints are the sterno-clavicular temporo mandibular and lumbar and dorsal spine Symmetrical involvement is common but when one side alone is affected this is the right side more often than the left The chief symptoms are pain stiffness and swelling of the affected joint which vary infinitely in degree Movement tends to aggravate the pain though stiffness may be worse after rest In more advanced cases there is marked swelling of the joint due both to thickening of the synovial membrane and effusion Accompanying the swelling there is invariably muscle weakness and atrophy apparently of greater degree than can be accounted for merely by disuse Finally the joints may become fixed or alternatively quite unstable owing to the extensive destructive process The fingers characteristically develop ulnar deviation with marked wasting of the small hand muscles

Subcutaneous nodules are occasionally found over bony surfaces In children rheumatoid arthritis is often associated with splenomegaly and lymphadenopathy (Still s disease) and these are sometimes found in adults Associated diseases are psoriasis occurring in some 2 or 3 per cent of subjects and persistent iritis which is more rare Amyloidosis has been reported to occur in some 10 per cent of advanced cases For long periods this may give rise to no symptoms and is merely responsible for albuminuria but the picture of the nephrotic syndrome occasionally develops and ultimately the patient may die from renal failure When albuminuria accompanies rheumatoid arthritis this possibility should be borne in mind and the matter can be pursued by the congo red absorption test The subjects of amyloidosis take up congo red injected intravenously much more completely than normal people

The disease varies infinitely in its course A complete remission may occur when the symptoms have only been mild and the patient is left with no disability and merely slight deformities of the joints At the other extreme steady progression takes place until virtually every joint in the body is ankylosed and the patient helpless Characteristically there are relapses and remissions which are of any length and type The relapses may be confined to the initially affected joints they may affect quite different joints or most often the initial joints and other joints Probably the average doctor has a much worse impression of rheumatoid arthritis than the reality because only the more severe cases seek medical advice Those who work in hospital tend in turn to see the worst of the cases occurring in general practice

Investigations. The E S R is always raised when the disease is active and there is a rough correspondence between the degree of rise and the severity of the symptoms But this adds little to the clinical picture Slightly hypochromic or normochromic anaemia is usual in severe cases but there is no precise relationship between its degree and the activity Sometimes there is an associated iron deficiency anaemia In the milder cases X ray changes are absent Later various changes such as translucency due to osteoporosis small cyst like areas of rarefaction narrowing of the joint spaces or subluxation may occur

Diagnosis In typical cases the diagnosis is obvious at a glance In the very mildest and earliest cases it may be impossible to reach a diagnosis In some acute cases it may be impossible to say whether the patient is best described as a case of rheumatic fever or of rheumatoid arthritis Typically osteo arthritis is quite different from rheumatoid arthritis though occasionally patients have features suggesting both conditions

Systemic lupus erythematosus which seems to be a definite clinical entity may present with polyarthritis suggesting rheumatoid arthritis but can be distinguished by the leucopenia haematuria pericardial or pleural involvement the discovery of L.E cells and other features This differentiation is important because lupus erythematosus responds well to steroids and has a worse prognosis Typical cases of the now rare gonococcal arthritis can be distinguished by their association with acute gonorrhoea and sometimes by the isolation of gonococci from the synovial fluid When chronic arthritis occurs in the subject with chronic gonorrhoea it may be impossible to determine whether the arthritis is gonococcal

Many attempts have been made to develop a reliable bio-chemical test for rheumatoid arthritis Most success has been achieved by the Rose Waaler test All human sera show agglutinating activity

against sheep red cells The serum of up to 90 per cent of cases of active rheumatoid arthritis causes this agglutination in a significantly higher titre if the cells have been sensitized by rabbit antibody whereas sera from patients with other conditions including ankylosing spondylitis rarely have this property But in the light of present knowledge the patient with the clinical features of rheumatoid arthritis who shows a negative result to the test should still be given the diagnosis of rheumatoid arthritis and treated in the same manner as those with the positive test Psoriatic arthritis is said always to be accompanied by a negative Rose Waaler test though as the clinical diagnosis of psoriatic arthritis is so obvious this observation while of theoretical interest helps little in practice Only in the rare case when a specific joint disease such as gonococcal or tuberculous arthritis or gout is suspect—and only the first named often causes difficulty—is the test likely to be of practical value since a positive result is strong evidence against these conditions Debating whether or not doubtful cases should be given the diagnosis of rheumatoid arthritis is as a rule diagnostic hair splitting which makes no useful progress

Treatment Nothing can be done to prevent the disease Because rheumatoid arthritis is a condition of infinitely varying natural history with relapses and remissions wrong conclusions about treatment are easily reached and a vast number of remedies have been claimed to be effective There is no good evidence that any remedies can influence the actual course of the disease except steroids and gold both of which have serious disadvantages and perhaps chloroquine

Rest and Exercise Such statements as the following are often seen in textbooks If those patients in the early stages of rheumatoid arthritis could be persuaded to give up work and take a rest cure *for 6 months or a year a much higher percentage* of them would make a complete and permanent recovery There is no evidence to support such statements No doubt many advanced cases were neglected in their early stages which leads to the quite unjustified deduction that if they had not been neglected they would not have become advanced The neglected cases who do not advance never seek medical advice

When the disease is acute and widespread the patient has no choice but to rest in bed and when one joint is acutely painful he will rest this joint by refraining from using it The important practical question is whether or not patients should be urged to rest to a greater degree than is dictated by their symptoms There is no evidence that the course of their disease will be favourably influenced by their so doing and prolonged rest in bed inevitably causes muscular wasting general weakness and decalcification of bones and encourages contractures apathy and depression On the other hand if a single joint is immobilized in plaster for a few weeks the patient s ability to carry out various activities may be improved and after the plaster has been removed the joint is often less swollen and painful and has an increased range of movement

If the actual disease process cannot be sensibly affected by rest the objects of both rest and exercise should be to discourage muscular wasting to prevent deformities to allow ankylosis in the most favourable position if this is inevitable to minimize disability and to encourage a hopeful attitude Because of the infinite variety of rheumatoid arthritis no standard recipe can be advocated but it seems that the general principles of treatment should be (1) Prolonged bed rest except in the most severe and generalized cases should not be used (2) When large joints are acutely painful they should be immobilized in plaster or other splint until the active process has subsided (3) Appropriate exercises should be carried out repeatedly This does not necessarily involve moving the joints quadriceps drill can be performed with the knee extended and when the painful wrist is immobilized in plaster fuller hand movements can be performed than would otherwise be possible (4) If deformity is developing suitable splints to overcome this while allowing the patient to use the affected limb should be used

Physiotherapy Heat massage and numerous other forms of passive physiotherapy are used very widely Evidence that they do good except perhaps in relieving pain is difficult to find In relieving pain they are probably inferior to the analgesic drugs and they encourage the idea in the patient that he must be made better not by his own efforts but by the efforts of others

Orthopaedic Procedures These are sometimes indicated in advanced cases with gross deformity but they have little if any place during the active phases of the disease Fixed deformities especially of the knees (which are most disabling) can sometimes be overcome by manipulation under an anaesthetic followed by immobilization in plaster Synovectomy may be useful when there is a proliferating mass of synovial membrane *Arthrodesis* can diminish the disability of a patient with an unstable and painful ankle or other joint

Diet Special diets have no proven value and the wasted patient with a poor appetite should be given tasty food which appeals to him rather than a *high calorie diet* which he will probably leave

largely uneaten Neither have vitamin supplements been shown to be beneficial

Climate Although rheumatoid arthritis is more common in a damp temperate climate than in a hot dry climate there is little evidence that after the disease has started residence in the latter kind of climate is valuable

Drugs Aspirin is the most generally useful drug Although it probably has little or no effect on the course of the disease it relieves the worst symptom —pain—and enables patients to live less handicapped lives than would otherwise be possible Up to 6 g (90 gr) daily or even more may be taken regularly in divided doses Similar amounts of calcium aspirin may be given to patients intolerant to aspirin Medical Research Council investigations in 1954 and 1957 suggested that among groups of patients with early rheumatoid arthritis aspirin was as effective as cortisone Yet many patients are unwilling to take these large doses of aspirin even when told that they will come to no harm but prefer to try a cure" such as gold even if told of its considerable hazards Efforts may therefore be needed to overcome this prejudice

Gold has been used in the treatment of rheumatoid arthritis for some 30 years but there is a good deal of uncertainty as to its value Controlled series have suggested but have hardly demonstrated beyond doubt that it favourably influences the course of the disease and it is often ineffective Moreover its hazards are open to no doubt toxic reactions occurring in some 40 per cent of patients though the great majority of these are trivial The *most serious reactions* which are all very rare but may be fatal are exfoliative dermatitis and agranulocytosis or aplastic anaemia More common and less serious are pruritus various skin eruptions stomatitis and albuminuria If the use of gold is contemplated the patient should be warned of these hazards and of the uncertainty of benefit. He should also be told to report any unusual symptoms and particularly skin irritation or eruptions or a sore throat. It is wise also to test the urine regularly for albumin

It nevertheless seems probable that gold can be of significant benefit sometimes In spite of these serious disadvantages its use may therefore be justified if the disease is active and advancing A widely used preparation is sodium aurothiomalate (Myocrisin) Doses are usually given weekly The initial amount is 10 or 20 mg rising to 50 mg and continuing until about 0 5 g has been given Further doses of 20 mg at 2 weekly intervals may then be given for a few months There is usually an interval of at least several weeks before improvement begins If after apparent benefit a relapse follows later another similar course may be given after an interval of some 6 months.

Chloroquine (and to a less extent other antimalarials) may induce remissions in a significant proportion of patients with rheumatoid arthritis Improvement may not occur for some 6–12 weeks Some 600 mg of chloroquine should be given daily though the dose may have to be lowered if there are gastric side effects If the drug seems effective it may be continued indefinitely in a maintenance dose of 200–400 mg daily

Steroid drugs will in large dosage quickly suppress the manifestations of rheumatoid arthritis But their long term effects are most disappointing If their administration is stopped the patient is apt to be left worse off than if he had never taken them If given indefinitely in large enough amount to suppress the symptoms to a useful degree serious side effects demanding a reduction in dosage often develop A balance has to be struck between the symptomatic relief and the side effects in adjusting the dose It has been noted that in M R C. investigations patients having cortisone did no better than those having aspirin It is therefore debatable whether steroids play a useful part in the treatment of rheumatoid arthritis At least, they should never be used for the mild case for the early case and for the long standing case with irreversible deformity and severe joint damage

If steroids are used they should be restricted to cases with widespread active and advancing disease who have not responded to such comparatively safe remedies as gold and chloroquine and who *do not obtain much symptomatic relief from regular* aspirin and suitable means for immobilizing joints. Because they cause fewer side effects prednisolone prednisone or triamcinolone should be preferred to cortisone The maintenance dose of prednisolone or prednisone which will cause worthwhile relief without severe side effects is usually in the region of 10–15 mg a day It is perhaps best to start with 15 mg daily and if the response is satisfactory to attempt reduction to 10 or less mg daily after some weeks Alternatively about 4/5 of these amounts of triamcinolone may be used We do not yet know what will happen to patients who continue to have these drugs for many years

Steroids injected into affected joints have no undesirable general side effects but can undoubtedly cause marked improvement at times On the other hand when weight bearing joints particularly the knee are injected there is a risk that by making the joint painless the patient will use it too much and destructive changes or even a Charcot type joint, may result. Patients with severe widespread disease are unsuitable for this kind of treatment

for obvious reasons The best cases are those who have one or a few large joints affected with minimal trouble elsewhere Following preliminary procaine and aspiration of synovial fluid (if present) 10–20 mg of prednisolone trimethyl acetate (which is perhaps the best preparation at present) or of 25 mg of hydrocortisone acetate or hydrocortisone tertiary butylacetate should be given These injections may be repeated every week or two according to the response

Phenylbutazone (Butazolidine) has a striking analgesic effect in many cases of rheumatoid arthritis (and of other varieties of arthritis) and sometimes seems superior to full doses of aspirin It has been thought to have some specific anti inflammatory effect similar to that of cortisone but this has not been proved When sufficient is given to produce satisfactory relief some 40 per cent of patients show side effects The most serious is agranulocytosis (which may be fatal) but this is very rare Another is haematemesis which is particularly common in patients with a history of peptic ulcer, but may occur in its absence The less serious side effects include the exacerbation of peptic ulcer symptoms or other kinds of dyspepsia sodium retention (which in minor degree is very common and sometimes causes overt oedema) soreness of the mouth (for which there is no apparent immediate cause) vertigo and rashes The serious reactions demand cessation of the drug but the minor ones do not The oedema of sodium retention can often be prevented or lessened by restricting the salt intake

Phenylbutazone should not be used in peptic ulcer subjects but otherwise a trial of it is justified when pain is severe in spite of full doses of aspirin 600 mg daily either taken at one time or in divided dosage should probably not be exceeded The dose should be reduced to the minimum which gives satisfactory relief this is often 200 or 400 mg daily If it seems valuable it can be continued indefinitely

Psychotherapy Widespread and severe rheumatoid arthritis is an unpleasant and depressing disease The depression can in turn aggravate the disability because the depressed patient is apt to make no effort to overcome his trouble and may develop contractures and become completely helpless The patient should be urged to do his utmost to overcome his disability though if the treatment advised involves a long spell of bed rest he cannot do this and talking to him is then unlikely to allay his depression In general the best antidote to depression is an active policy of treatment such as has been advocated by analgesic drugs suitable immobilization and splintage and encouragement to remain at work If prolonged bed rest cannot be avoided occupational therapy may help to combat depression

Treatment of Associated Anaemia The moderate normochromic or slightly hypochromic anaemia which accompanies active rheumatoid arthritis is responsive to no treatment except blood transfusion the effect of which is temporary When as is often the case there is associated iron deficiency anaemia iron should be given It may be effective by mouth but if it is not saccharated oxide of iron (Ferrivenin) should be given intravenously in doses of about 5 ml (containing 100 mg elemental iron) twice a week or a dextran iron complex (Imferon) in doses of about 5 ml (containing 250 mg ferric hydroxide) given deeply into the glutei twice a week The total amount of iron needed can be calculated from the degree of iron deficiency anaemia and this amount should not be much exceeded

A Rheumatoid Syndrome without Joint Disease

A quite common syndrome which affects the elderly especially and is characterized by widespread muscular pain and constitutional disturbance has been given the name "polymyalgia rheumatica (Barber 1957) It has also been described as anarthritic rheumatoid disease (Bagratuni 1956)

Clinical Picture The syndrome may start as a pyrexial illness with sweating loss of appetite and weight malaise generalized muscular aching especially in the neck shoulders and back and often headache The patient may look generally ill but otherwise there are no definite signs apart sometimes from muscle tenderness and perhaps pain on moving the neck and back Rheumatic nodules or rashes are seen occasionally There is no evidence of joint disease beyond transient swellings in a few cases

The most striking laboratory finding is the very high E S R —usually above and often much above 100 mm in 1 hr (Westergren) There is also a moderate iron resistant normochromic or hypochromic anaemia a high plasma fibrinogen level and usually an increase in the globulin fraction and a decrease of the albumin fraction of the plasma proteins

The syndrome usually persists for months or a few years often with remissions In the end complete recovery seems to occur the lost weight being regained the anaemia clearing up and the E S R falling to normal

Diagnosis When patients with this syndrome are first seen they present a difficult diagnostic problem as the clinical picture is similar to that of some such occult malignant disease as osseous secondary deposits or deep seated Hodgkin s dis

ease and also to that of systemic lupus erythematosus. The fever may even suggest an infection and much futile effort may be expended in attempting to isolate an organism Sometimes only the lapse of time will make it certain that the process is benign and it is then easy to recognize the syndrome if its existence is known.

Treatment. As a rule the only treatment needed is aspirin or perhaps phenylbutazone for the relief of pain and reassurance about the future In severe cases it may be justifiable to give small doses of steroids such as prednisolone 5 mg b d which appear very effective

Ankylosing Spondylitis

Although in common with the other rheumatic conditions there are border line and doubtful cases ankylosing spondylitis forms a definite clinical entity There has been much debate as to whether or not it should be considered as separate from rheumatoid arthritis or as a variant of this condition As long as our ignorance of the aetiology of the rheumatic disorders persists such debate is unfruitful The condition has been recognized for a long time Connor in 1691 described a skeleton "where vertebrae the ribs and several bones down to the os sacrum were all firmly united into one solid bone without joynting or cartilage But because it was confused with other disorders only recently has it been considered a satisfactory entity

The aetiology of ankylosing spondylitis is unknown It is about 10 times commoner in men than women and its onset is usually between the ages of 15 and 40 The process usually begins in the sacro iliac joints and spreads to the posterior inter vertebral and costo vertebral joints But occasionally peripheral joints are initially involved especially the hips knees and ankles Iritis accompanies the disease sometime in its course in some 20 per cent of cases

Clinical Picture The onset is usually insidious with pain in the lower back often radiating into the thighs The pain may begin in the neck and shoulders or occasionally in peripheral joints and there may also be widespread fleeting pains in various places The pain is made worse by movement of the spine and often by coughing Its severity varies infinitely Some degree of stiffness is usual from the start. If the costovertebral joints are involved the chest becomes deformed and its movements restricted with consequent effort dyspnoea and a liability to respiratory infections In the earlier phases such general symptoms as malaise loss of weight, low grade fever and tachycardia are common

In many patients the disease relentlessly advances until the spinal joints become ankylosed and the anterior and lateral ligaments become calcified As the ankylosis progresses the pain declines and in the end may disappear The general symptoms of ill health also diminish In severe cases complete rigidity of the spine with variable degrees of kyphosis develops within 3 years in milder cases this may take up to 25 years Sometimes permanent remission occurs before the spine is fully involved and even before it has extended beyond the sacro-iliac joints Occasionally after a prolonged remission there is reactivation though as a rule exacerbations and remissions are less striking than in rheumatoid arthritis and may never occur

Investigations. Radiological changes are slight in the initial phases They usually occur first in the sacro iliac joints which show haziness and narrowing of the joint spaces Later there is decalcification of the vertebral bodies and finally calcification may be seen in the anterior and lateral spinal ligaments

A rise in the E.S R often to a very high level, is invariable in the active phase Some degree of normochromic or hypochromic anaemia is common

Diagnosis. Because the onset is often so insidious the condition may not be recognized for a long time the subject merely being thought to have some ordinary variety of backache But if suspected the diagnosis is not usually difficult and is made from the persistent pain in the lower back the flattening and loss of movement of the lumbar spine and the X ray appearances The raised E.S R and anaemia are further suggestive features

Treatment. There are no known means of preventing the disease and no remedy has any proven effect in altering its course The most popular treatment is radio therapy to the affected region of the spine which without reasonable doubt can markedly relieve the pain of the active phase It has been claimed that radio therapy may in some cases arrest the progress of the condition but this is unproven The incidence of leukaemia among subjects treated by radio therapy seems to be between 5 and 10 times that of the general population Although those with ankylosing spondylitis may be unduly susceptible to leukaemia the radio-therapy is probably responsible at least in part for this increased incidence Only one course therefore should be given especially as further courses are usually much less effective than the first

In so far as radio therapy is not used or is ineffective regular analgesic drugs should be given Phenylbutazone has been claimed to be particularly effective here and should be used if aspirin gives imperfect relief

There is no evidence that the prolonged immobilization which used to be favoured is beneficial. It

is doubtful whether deformity can be prevented but with that end in view it seems reasonable to advise the patient to sleep on a firm flat bed with a low pillow and to perform regular extension exercises for the back Breathing exercises may also help If severe fixed kyphosis develops spinal *osteotomy may be indicated*

If there is iron deficiency anaemia this should be treated by iron by mouth or if that is ineffective by intravenous or intramuscular iron *Special diets* and other general measures of treatment have no proven value

Systemic Lupus Erythematosus

A rare generalized chronic disease affecting the connective tissues It occurs predominantly in young and middle aged women runs a variable course and ultimately is usually fatal It has become increasingly recognized in recent years though this is at least partly due to a greater awareness of its existence it is questionable whether the true incidence has increased Its relation to the skin condition chronic discoid lupus erythematosus which is usually benign and may remain unchanged for years or clear up has been disputed but both are *probably varieties of the same basic process* Some 20 per cent of those with systemic lupus erythematosus are said to give a previous history of the localized skin disease Neither of the two forms has any connexion with lupus vulgaris

Aetiology The essential cause of the disease is unknown It has been suggested that it may be a hypersensitivity reaction to bacterial products (in the same way as rheumatic fever is a reaction to haemolytic streptococci) but this is unproven Sulphonamides and antibiotics which have been used on such an enormous scale in recent years may possibly be aetiological factors Heavy exposure to *sunlight sometimes precipitates though it can* not be said to cause the disease Recurrences may also follow exposure to sunlight

Pathology By comparison with the extent and severity of the clinical features the gross pathological changes are usually slight The essential lesion would seem to be a widespread degenerative process in the connective tissues with proliferation of fibroblasts This may result in necrosis of the small vessels The pericardium pleura heart lungs spleen liver kidneys *lymph nodes and skin may* all be involved

Clinical Picture The disease usually appears in a *previously* healthy young or middle aged woman though it is sometimes preceded by chronic benign discoid lupus erythematosus and sometimes by what seems to be typical rheumatoid arthritis which may have been present for years The onset may be most insidious or quite acute the picture varies very widely and remissions and exacerbations of all sorts may occur

The presenting complaint may be any of the following malaise fever weight loss skin rash painful or swollen joints enlarged lymph glands pain on breathing or praecordial pain After a few weeks the symptom may disappear and any time later the same or a different symptom may return *Depending on the symptoms examination may* reveal (1) A rash This commonly appears on the exposed parts of the face and upper chest though may later be widespread *There are erythematous* macules or papules which become confluent, and later there may be telangiectases (2) Polyarthritis which suggests rheumatic fever or rheumatoid arthritis (3) Splenomegaly (4) Enlarged lymph glands (5) A pleural or pericardial rub or signs of effusion (6) Albuminuria, microscopic haematuria or casts (7) In severe cases a general toxic state with high fever and often gallop rhythm

The course of the disease varies from weeks to several years and in nearly all recognized cases death has ultimately occurred though there may be remissions of up to a few years The final cause *of death may be renal failure cardiac failure* pneumonia or cerebral or gastro intestinal haemorrhage Treatment can probably prolong life

Investigations Some degree of normochromic anaemia is usually present There is also leucopenia moderate as a rule and sometimes thrombocytopenia Plasma globulin is often increased and the albumin globulin ratio may be reversed The E S R is typically greatly increased The lupus erythematosus cell or L E cell of Hargraves may be demonstrated in the peripheral *blood or marrow* This is a polymorphonuclear leucocyte containing a round inclusion of nuclear material staining deep *blue with haematoxylin* These cells can also be formed by adding affected patients serum to normal marrow cells A false positive serological test for syphilis is fairly common

Diagnosis Because of the greatly varying manifestations this is difficult especially when no skin eruption is present Unless the disease is constantly borne in mind the diagnosis is apt to be missed It should be especially suspect when there is prolonged fever polyarthritis which is not typical of *rheumatoid arthritis or unexplained pleurisy* or pericarditis The discovery of the L.E cell is a strongly suggestive diagnostic pointer

Treatment Steroid drugs will undoubtedly suppress the manifestations of the disease If the case is mild and especially in periods of remission these drugs should not be used but when the symptoms are severe *full amounts should*

be given 300 mg of cortisone or 60 mg of pred nisone daily are usual starting doses though much larger amounts may be needed to suppress the fever and other symptoms If after a few weeks the patient remains symptom free the dose should be *gradually reduced* and the *minimum* amount to control the symptoms maintained It may be pos sible to withdraw the drug altogether though a relapse will occur after some weeks months or occasionally years when it does the drug may be restarted It seems likely that life can be prolonged in this way Mepacrine which is so useful for dis coid lupus also appears to benefit patients with the systemic disease A maintenance dose of about 400 mg daily may be given for prolonged periods It should perhaps be used for the milder cases and especially when arthritis and skin lesions are promi nent as they are said to be more responsive than other lesions Mepacrine may also be combined with steroids If secondary infections occur antibiotics may be valuable and if anaemia is severe trans fusion is possibly justified Diet and the degree of activity can be left to the patient s inclination

Dermatomyositis

A rare disorder of unknown aetiology involving skin and muscle and affecting both sexes and all ages equally It is sometimes secondary to malignant disease especially of the breast or ovary though the explanation of this development is quite obscure

Pathology The affected muscle is pale and oedematous There is degeneration of the muscle fibres and infiltration with lymphocytes and large mononuclear cells Later there is fibrous tissue replacement The skin may show changes suggesting scleroderma

Clinical Picture The onset is usually insidious but occasionally sudden Common early symptoms are weakness muscle tenderness oedema and an erythematous skin eruption often on the face and neck When the onset is acute there may be fever and profound malaise The variety which is secon dary to malignant disease is usually acute Some times the disease is preceded by manifestations suggesting rheumatic fever or rheumatoid arthritis

The course of the disease is infinitely variable There may be rapid deterioration and death in a few weeks especially when the onset is acute but more often the process becomes arrested or pro gresses only very slowly for years Death is the usual final outcome though a few minor cases may remain stationary indefinitely For long periods there may be only slight disability but in more severe cases there is great weakness and the patient is bedridden In the later stages there may be atrophy or telangiectasia of the skin and sometimes the picture of scleroderma develops

The only investigation of much value (other than those for elucidating associated malignant disease if this is present) is muscle biopsy though a single normal biopsy does not exclude the disease

Treatment Steroid drugs in full dosage are prob ably life saving in the acute forms of the disease and after their gradual withdrawal there may be a prolonged remission These drugs are much less effective in the chronic form and may apparently be useless If a malignant tumour is present this should if possible be removed a remission of the dermatomyositis may then follow

Erythema Nodosum

A fairly common skin eruption accompanied by fever and constitutional upset usually secondary to some infection It is most frequent in children and young adults

The most commonly demonstrated infection which provokes erythema nodosum is primary tuberculosis it is responsible for some 75 per cent of cases in children and 25 per cent in adults The next most common is a streptococcal throat infec tion others are secondary syphilis gonorrhoea and meningococcal and staphylococcal infections It may also be associated with sarcoidosis and is pos sibly provoked by certain drugs especially sul phonamides Frequently no causative infection can be identified and epidemics of this type have occurred

Histological examination shows capillary dilata tion and extravasation of serum leucocytes and red cells into the surrounding tissues The bruised appearance in the healing stage is due to red cell disintegration

Clinical Picture The eruption consists of circu lar or oval lesions from about ½ to 5 cm across and red or purple in colour They occur most on or near the shins but sometimes also on the thighs buttocks or extensor surfaces of the arms and forearms They are tender and usually painful and the overlying skin is smooth and shiny In children the lesions are often more numerous and smaller than in adults There may be one or several crops of lesions and the total duration of the process is usually several weeks but may be less

Mild constitutional symptoms may precede the eruption and it is associated with more or less malaise and fever a markedly elevated E S R and sometimes painful joints which may be swollen

Treatment Appropriate remedies should be given for the underlying infection if present There is no evidence that this or any other treatment affects

is doubtful whether deformity can be prevented but with that end in view it seems reasonable to advise the patient to sleep on a firm flat bed with a low pillow and to perform regular extension exercises for the back Breathing exercises may also help If severe fixed kyphosis develops spinal osteotomy may be indicated

If there is iron deficiency anaemia this should be treated by iron by mouth or if that is ineffective by intravenous or intramuscular iron Special diets and other general measures of treatment have no proven value

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Pathology By comparison with the extent and severity of the *clinical features the gross patho*logical changes are usually slight The essential lesion would seem to be a widespread degenerative process in the connective tissues with proliferation of fibroblasts This may result in necrosis of the small vessels *The pericardium pleura heart lungs* spleen liver kidneys lymph nodes and skin may all be involved

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Diagnosis Because of the greatly varying manifestations this is difficult especially when no skin eruption is present Unless the disease is constantly borne in mind the diagnosis is apt to be missed It should be especially suspect when there is pro*longed fever polyarthritis which is not typical* of rheumatoid arthritis or unexplained pleurisy or pericarditis The discovery of the L E cell is a strongly suggestive diagnostic pointer

Treatment Steroid drugs will undoubtedly suppress *the manifestations* of the disease If the case is mild and especially in periods of remission these drugs should not be used but when the symptoms are severe full amounts should

the cartilage becomes worn away at first in the centre exposing the subchondral bone This becomes hyperplastic with a sclerosed irregular and widened surface At the same time proliferative changes occur at the margins of the joints with cartilaginous excrescences which calcify to form osteophytes When on the dorsum of the bases of the terminal phalanges these osteophytes are called Heberden s nodes The villi of the synovial membrane increase in size and number and become congested with red cells or loaded with fat later they may calcify and break off into the joint cavity forming loose bodies

In the spine osteo arthritis with changes similar to those of the limb joints occurs in the apophyseal joints The antero lateral osteophytes which are almost universal in late adult life and cause the radiological changes described as osteo arthritis are thought to follow degenerative changes in the intervertebral discs

Clinical Picture Since nearly all old people develop some of the changes of osteo arthritis these changes do not necessarily cause symptoms There is moreover no relation between the severity of the symptoms and the severity of the process as assessed radiologically gross X ray changes may be associated with no symptoms and minimal changes with severe symptoms Symptomatic remissions which may be permanent are common

The commonest clinical manifestation of the ordinary variety of osteo arthritis are Heberden s nodes—small knobs developing insidiously on the dorsal surface of the terminal phalanges just beyond the distal interphalangeal joints of the fingers Their main ill effect is to cause disfigurement The associated changes in the distal interphalangeal joints may be symptomless but may be accompanied by some pain and stiffness In later stages marked lateral deviation of the terminal phalanges may occur Other commonly affected joints are the knees hips metatarso phalangeal joint of the big toe carpo metacarpal joint of the thumb and the acromio clavicular joint The metacarpo phalangeal joints the elbows wrists and ankles are rarely affected sufficiently to cause symptoms

The supreme symptom is pain which usually develops insidiously and is worsened by movement As a rule the pain is chiefly felt in the region of the joint but the pain of hip joint disease is commonly referred to the thigh or to the knee and is often severe when the patient is in bed The other main symptom is joint stiffness which is of infinitely variable degree This is often a striking feature of hip joint disease the hip may be almost fixed or in less advanced cases there is limitation of external rotation and abduction Grating sensations are often complained of by introspective subjects or may be felt by the examiner when moving joints are palpated If intra articular loose bodies develop—as they often do in the knee—clicking or transient locking on movement may occur In advanced cases the knee may be grossly disorganized More or less muscular wasting and weakness are invariable when the process is severe

The first radiological change is a narrowing of the joint space Later the articular surface may be irregular there is gross marginal lipping and osteophyte formation and the joint space may be completely obliterated The subchondral bony layer remains dense but elsewhere the bone may be decalcified

No characteristic laboratory findings develop there being no anaemia or rise in the E S R

The syndrome which has been called primary generalized osteo arthritis (Kellgren and Moore) is different in many ways from the varieties already considered It occurs predominantly in middle aged women Heberden s nodes with affection of the distal interphalangeal joints are very common The first carpo metacarpal the proximal interphalangeal and the foot joints (especially the first metatarso phalangeal) are also frequently involved The large joints are much less often affected The striking feature of the syndrome is the initial acute phase in which the joint is warm red extremely tender and often swollen with a small effusion There may be severe spontaneous pain Numbers of joints may be affected simultaneously by this acute process or they may be affected in turn over the course of months or years The acute phase subsides after some months and is followed by a chronic phase with massive bony outgrowths and unsightly deformity but with little pain and disability During the acute phase the E S R is often moderately elevated to a figure in the region of 20 mm after 1 hr (Westergren) or sometimes higher

Diagnosis In typical cases there is no diagnostic problem Because osteo arthritis of the hip may cause pain down the leg it may be wrongly diagnosed as sciatica but the restricted hip movements and the aggravation of pain by attempting to move the joint in all directions should make the diagnosis clear The generalized variety of osteo arthritis in its acute phase may suggest rheumatoid arthritis but the absence of affection of the metacarpo phalangeal joints the special affection of the distal interphalangeal joints and the absence of severe constitutional symptoms should make the differentiation This is of some importance if only by making it possible to reassure those with osteo arthritis about their future

the course of the erythema nodosum Analgesics may be required and if the patient is ill it may be desirable to keep him in bed for a time

Erythema Multiforme

A variable skin eruption associated with more or less constitutional upset *and often with mucous* membrane lesions It has been said to be secondary to streptococcal and other infections drugs toxic products of food and other factors though in practice a convincing underlying condition can rarely be identified Moreover it is dangerous to deduce that because a patient has erythema multi forme and say a septic focus the one is the cause of the other The disorder is said to be most common in spring and autumn and recurrent *attacks may occur especially at these times of the* year

Histologically there is inflammation of the super ficial layer of the corium with cellular infiltration especially around the vessels and oedema of the prickle cell layer

Clinical Picture The eruption is variable as the name of the condition implies It may be macular papular circinate or occasionally bullous or pur puric and tends to be most marked on the dorsal surfaces of the hands and feet and on the forearms legs and face Lesions in the mouth are fairly com mon and on the eyes and genitalia occasional The *process usually lasts from a few days to a few weeks* but sometimes longer There may be few or no constitutional symptoms or a mild or moderate fever and general malaise

A much more severe variety of erythema multi forme known as the Stevens Johnson syndrome has been frequently described in recent years and epidemics have occurred There is a widespread bullous eruption the whole mouth may be intensely inflamed and purulent the eyes closed from oedema of the lids and *conjunctival inflammation and the* anus extensively affected In addition severe consti tutional upset with a high swinging fever anaemia and rapid loss of weight occur The disorder may last from two to several weeks and relapses sometimes occur Fatalities from toxaemia or pneumonia are not uncommon. Severe permanent impair *ment of vision may result from corneal scarring* There may also be scarring of the skin though considering the severity of the acute process this is usually surprisingly slight

Diagnosis. If the disorder is suspected diagnosis both of the ordinary form and the Stevens Johnson syndrome is usually simple The course of the process and *the absence or* slight nature of perma nent damage to the skin are other clues Ringworm pityriasis rosea pemphigus dermatitis herpeti formis and secondary syphilis may possibly be suspected in the early stages

Treatment No remedy has a proven effect on the course of the process For the mild cases no treat ment beyond reassurance is indicated Subjects of the Stevens Johnson syndrome may be so ill as to *need a great deal of nursing* Their mouths may be so sore as to make feeding difficult and tube feeding may be advisable Although antibiotics do not influence the essential *process it seems reason* able to give them with the idea of preventing secondary infection Blood transfusion is probably justified if marked anaemia develops Symptomatic remedies for the relief of pain and insomnia and mouth washes to relieve the distressing mouth con dition are often needed

Osteo-Arthritis

A non specific degenerative process of joints is given the *name osteo arthritis although* there is usually no evidence of an inflammatory process and there are few or no constitutional symptoms A generalized and often fairly acute joint disorder associated with signs of inflammation is also des cribed as osteo arthritis Both varieties particularly affect subjects in late adult life though they occa *sionally occur at a younger age*

Aetiology As people age the hyaline cartilage of their joints develops degenerative changes The *extent of this process varies greatly* and it usually occurs first in the weight bearing joints Changes which can be described as osteo arthritis" are therefore universal in old age Joints which have been damaged or are apparently subject to undue strain are particularly affected Such strain" may affect the knee joints of those with genu varum or *valgum or various joints of people with muscular* weakness resulting from disease of the central nervous system Otherwise no convincing explana *tion of the development of osteo arthritis* in a par ticular joint can usually be found The disorder is common among the obese, which can be explain d by the greater strain to which their joints are subject Infective foci endocrine *disorders* and other factors have been incriminated but there is no evidence to support such theories and even if they are true they do not explain why certain joints only should be affected The generalized form of osteo arthritis on the other hand has features sug gesting that some general agent is at work but this agent has not been identified

Pathology The first change is said to be a softening of the articular cartilage which loses its shiny surface and becomes dull and opaque The surface tends to peel off in small flakes the deeper layers split, and the cartilage cells become necrotic In consequence

periods when they seem normal The knees are much the most commonly affected and the condition is often bilateral It usually begins in middle life For no apparent reason the joints fairly suddenly swell with a synovial effusion and varying degrees of pain but with little evidence of inflammation After some 3 to 5 days the process subsides and there is then a symptom free period of 3 to 30 days The periodicity is fairly constant as a rule in each individual patient Attacks may continue for years though sometimes there are long remissions In the end they may cease entirely though occasionally the picture of rheumatoid arthritis ultimately supervenes Pathologically there is chronic inflammation of the synovial membrane with lymphocytic infiltration and proliferation of the villi and the effusion contains numerous lymphocytes and polymorphs No treatment has any certain effect on the course of the process though hydrocortisone injections into the affected joint and radiotherapy are sometimes apparently successful During the episodes when the joints are swollen a spell in bed may be advised or a firm bandage applied

Reiter's Syndrome This rare syndrome comprises arthritis urethritis and conjunctivitis occurring simultaneously The aetiology is unknown Both the urethritis and the conjunctivitis are purulent but no specific organism has been identified The conjunctivitis may be associated with iritis and keratitis The arthritis is multiple tends to involve the larger joints in sequence rather than concurrently and is accompanied by a sterile purulent effusion The only disorder which is likely to be confused with it is gonorrhoea with gonococcal arthritis from which it is distinguished by the absence of gonococci and the negative complement fixation test Recovery is usually complete after a course of a few weeks to several months though there may be recurrences years later Fever therapy with the hypertherm is said to be beneficial other remedies have no proven effect on the course of the process

The Painful Shoulder

The shoulder joint may be affected by rheumatoid arthritis rheumatic fever acute infective arthritis tuberculosis fracture and other more or less well defined pathological or clinical syndromes Pain in the region of the shoulder may also be referred and due to lesions elsewhere These lesions can be grouped under three heads (1) Diseases of the central nervous system such as spinal cord tumours They are a rare cause of shoulder pain (2) Conditions affecting the nerve roots or brachial plexus The most common is probably a prolapsed cervical intervertebral disc others are ankylosing spondylitis cervical rib and the costo-clavicular syndromes and secondary neoplasm (3) Various visceral diseases Coronary artery disease may be responsible for pain in the left shoulder region and liver and gall bladder disease for pain in the right shoulder region All these referred pains are commonly felt in the arm and sometimes in the forearm and hand as well as in the shoulder

Most pain in the shoulder region is due to none of these causes but to disorders of the structures surrounding the joint These disorders seem to have no counterpart in the periarticular structures of the other joints and they therefore warrant this special section Their aetiology is often obscure and there has been much dispute as to the precise pathological changes but some clinical syndromes are fairly definite All these syndromes occur particularly in the middle aged and elderly and all seem to be related to the degenerative changes of advancing years The tendons subserving the shoulder joint become increasingly adherent to the capsule until in old age there may be complete fusion These changes are most marked in the upper part of the capsule the supraspinatus tendon and the upper parts of the sub-scapularis and infraspinatus tendons being intimately fused with each other and with the capsule by middle life Degenerative changes ranging up to complete rupture of this fused structure are increasingly common as age advances Some degree of rupture is found in over half those older than 75 Other factors which may contribute to the clinical syndromes are trauma and immobilization But these factors do not satisfactorily explain all the clinical features of those with painful shoulders

Frozen Shoulder This is a fairly common condition in which there is little or no movement at the shoulder joint This may not be obvious with superficial examination because of movement of the whole shoulder girdle Some cases are clearly precipitated by trauma and others by immobilization which itself is often secondary to pain in the shoulder and this pain may be traumatic Another important cause of immobilization is a hemiplegia from a cerebral vascular accident There may be complete recovery of the hemiplegia but the shoulder remains frozen this being the chief residual disability Sometimes the condition follows cardiac infarction Many cases of frozen shoulder develop without any apparent precipitating cause sometimes insidiously and sometimes fairly acutely One shoulder is most often affected but bilateral trouble is not uncommon The average age of onset is about 55

Pain is the main initial symptom which may be intense and nearly continuous and often spreads down the arm In addition to the lack of movement there may be some swelling of the shoulder and

A common diagnostic error is the wrong attribution of pain to the "osteo arthritic changes seen in radiographs This particularly occurs with backache and osteo arthritis of the spine is nearly always an improper diagnosis because the pain is not related to the X ray changes These changes moreover, are seen in a high proportion of old people who are free of backache Pain may also be wrongly ascribed to the osteo arthritic X ray changes in the hip joint when in fact it is due to 'sciatica resulting from a spinal lesion With the other joints this error is unlikely to be made

The changes of osteo arthritis may co-exist with rheumatoid arthritis fairly often The attempt to decide what proportion of the mischief is caused by each of these disorders is unprofitable

Treatment. No remedy has an appreciable effect on the course of the process The obese seem to be unduly liable to osteo arthritis of the weight bearing joints and their obesity aggravates the disability due to the arthritis so there are strong grounds for urging weight reduction If walking causes pain the patient will walk little there are no good grounds for advocating rest of any greater degree Heat is widely used in the form of hot baths for the hands short wave diathermy for larger joints and such domestic remedies as hot water bottles But the relief of pain given by heat is probably much less than that given by aspirin When there is much muscular wasting exercises—if the joint condition allows them—are beneficial to the muscles though not to the joints The most generally useful remedy is aspirin or other analgesic drugs which relieve the main symptom of the disorder—the pain

A procedure which is well worth a trial is the intra or periarticular injection of procaine Lactic acid and other substances have been used with procaine but whether they have any advantages over procaine alone seems doubtful Perhaps the knee joint is the most suitable If the first injection seems to give relief further injections may be continued at weekly or two weekly intervals indefinitely Sometimes the mobility of a joint is apparently improved by this procedure Hydro cortisone or other steroid injections (as described under rheumatoid arthritis) may also be used and may be more effective than procaine though they are probably less effective than in rheumatoid arthritis

When the pain from osteo arthritis of the hip is very severe and imperfectly relieved by analgesic drugs operation may be considered The simplest operation is arthrodesis which is done by inserting a Smith Petersen pin through the head of the femur into the acetabulum or by more elaborate procedures If successful the hip is left permanently stiff but painless Arthroplasty operations in which a new hip joint is fashioned by a vitallium cup or acrylic resin prosthesis (Judet s operation) have the great advantage if successful of restoring mobility to the hip but the disadvantage that in the course of time the prosthesis may break or the cup give trouble perhaps leaving the patient in a most unhappy situation Loose bodies in osteo arthritic knee joints which cause pain and locking may be removed surgically Unstable knee joints may be supported by appliances and if very painful may be immobilized in plaster of paris for a time, often with prolonged relief Painful ankle joints may be ankylosed

In treating the acute phase of the generalized variety of osteo arthritis analgesic drugs are especially valuable When one or two distal interphalangeal joints are acutely painful and tender immobilization with small plaster of paris casts for a few weeks relieves pain and enables the hands to be used more effectively When the plaster is removed the acute process may have subsided

Patients are apt to fear that they are in the grip of a progressively-disabling disease especially when affected by the generalized variety of osteo arthritis A statement that nothing worse than minor disability is to be anticipated and that the acute widespread process will subside in time merely leaving distorted but painless joints may be most reassuring Patients should also be encouraged to go about their usual affairs as far as they can

Rare Non specific Varieties of Arthritis

There are a few well defined syndromes which seem to be distinct both from rheumatoid arthritis" and osteo arthritis

Charcot s Joints These develop in the subjects of chronic neurological diseases which cause sensory loss and weakness Tabes dorsalis and syringomyelia are the most common One or two large joints are usually affected the knee or hip most often in tabes and the shoulder or elbow in syringomyelia Initially there is a painless serous effusion and later thickening of the synovial membrane and destruction of the joint surface and the nearby bone Ultimately the joint may become completely disorganized flail like and greatly enlarged with loose bodies in the joint and osteophytes around Throughout a striking feature is the absence of pain (which is due to the underlying neurological disease) The diagnosis is simple provided the neurological disease is recognized No treatment affects the course of the process and all that can be done is to support the joint by suitable apparatus

Intermittent Hydrarthrosis This is a very rare but most remarkable condition in which there are recurrent effusions into the joints with intervening

periods when they seem normal The knees are much the most commonly affected and the condition is often bilateral It usually begins in middle life For no apparent reason the joints fairly suddenly swell with a synovial effusion and varying degrees of pain but with little evidence of inflammation After some 3 to 5 days the process subsides and there is then a symptom free period of 3 to 30 days The periodicity is fairly constant as a rule in each individual patient Attacks may continue for years though sometimes there are long remissions In the end they may cease entirely though occasionally the picture of rheumatoid arthritis ultimately super venes Pathologically there is chronic inflammation of the synovial membrane with lymphocytic infil tration and proliferation of the villi and the effusion contains numerous lymphocytes and polymorphs No treatment has any certain effect on the course of the process though hydrocortisone injections into the affected joint and radiotherapy are sometimes apparently successful During the episodes when the joints are swollen a spell in bed may be advised or a firm bandage applied

Reiter s Syndrome This rare syndrome comprises arthritis urethritis and conjunctivitis occurring simultaneously The aetiology is unknown Both the urethritis and the conjunctivitis are purulent but no specific organism has been identified The con junctivitis may be associated with iritis and kera titis The arthritis is multiple tends to involve the larger joints in sequence rather than concurrently and is accompanied by a sterile purulent effusion The only disorder which is likely to be confused with it is gonorrhoea with gonococcal arthritis from which it is distinguished by the absence of gonococci and the negative complement fixation test Recovery is usually complete after a course of a few weeks to several months though there may be recurrences years later Fever therapy with the hypertherm is said to be beneficial other remedies have no proven effect on the course of the process

The Painful Shoulder

The shoulder joint may be affected by rheumatoid arthritis rheumatic fever acute infective arthritis tuberculosis fracture and other more or less well defined pathological or clinical syndromes Pain in the region of the shoulder may also be referred and due to lesions elsewhere These lesions can be grouped under three heads (1) Diseases of the central nervous system such as spinal cord tumours They are a rare cause of shoulder pain (2) Condi tions affecting the nerve roots or brachial plexus The most common is probably a prolapsed cervical intervertebral disc others are ankylosing spondy litis cervical rib and the costo clavicular syn dromes and secondary neoplasm (3) Various visceral diseases Coronary artery disease may be responsible for pain in the left shoulder region and liver and gall bladder disease for pain in the right shoulder region All these referred pains are com monly felt in the arm and sometimes in the fore arm and hand as well as in the shoulder

Most pain in the shoulder region is due to none of these causes but to disorders of the structures surrounding the joint These disorders seem to have no counterpart in the periarticular structures of the other joints and they therefore warrant this special section Their aetiology is often obscure and there has been much dispute as to the precise pathologi cal changes but some clinical syndromes are fairly definite All these syndromes occur particularly in the middle aged and elderly and all seem to be related to the degenerative changes of advancing years The tendons subserving the shoulder joint become increasingly adherent to the capsule until in old age there may be complete fusion These changes are most marked in the upper part of the capsule the supraspinatus tendon and the upper parts of the sub scapularis and infraspinatus tendons being intimately fused with each other and with the capsule by middle life Degenerative changes rang ing up to complete rupture of this fused structure are increasingly common as age advances Some degree of rupture is found in over half those older than 75 Other factors which may contribute to the clinical syndromes are trauma and immobilization But these factors do not satisfactorily explain all the clinical features of those with painful shoulders

Frozen Shoulder This is a fairly common con dition in which there is little or no movement at the shoulder joint This may not be obvious with superficial examination because of movement of the whole shoulder girdle Some cases are clearly pre cipitated by trauma and others by immobilization which itself is often secondary to pain in the shoulder and this pain may be traumatic Another important cause of immobilization is a hemiplegia from a cerebral vascular accident There may be complete recovery of the hemiplegia but the shoul der remains frozen this being the chief residual disability Sometimes the condition follows cardiac infarction Many cases of frozen shoulder develop without any apparent precipitating cause sometimes insidiously and sometimes fairly acutely One shoulder is most often affected but bilateral trouble is not uncommon The average age of onset is about 55

Pain is the main initial symptom which may be intense and nearly continuous and often spreads down the arm In addition to the lack of movement there may be some swelling of the shoulder and

the impression given is of an active inflammatory process In time the pain subsides and the shoulder is left stiff and painless except when movement is attempted The course of the process can thus be divided into an irritative and an adhesive stage After a further period there may be spontaneous return of movement and ultimately complete recovery may occur though probably in not more than about half the cases *Some may recover partially* still being left with various degrees of stiffness pain and weakness A few do not recover at all and develop gross wasting of the shoulder muscles

Treatment Shoulders which are immobilized as the result of hemiplegia and other non painful states should be regularly put through a full range of movement in the hope of preventing the freezing up process *Injured shoulders should be moved* to the extent which pain allows though there is the risk that movement may do further damage The attempt to move the shoulder affected by the spontaneous variety of the disorder in the acute irritative phase seems to be at best futile and at worst *followed by extreme pain and an aggravation of* the process Here the right course is to leave the shoulder well alone or possibly provide a sling for support and give the patient analgesic drugs Heat and other local applications are probably useless If after the acute phase has subsided there is no sign of spontaneous return of movement, active steps may be considered and the same steps may be taken when the frozen shoulder has followed trauma or immobilization A simple measure is the injection of procaine into the capsule at about weekly intervals Sometimes this is followed by a gradual return of movement perhaps as the result of the self manipulation made possible by the temporary anaesthesia Injections of steroid drugs have been widely used but there have been most conflicting reports as to their value If these methods are ineffective manipulation under anaesthesia may be considered This should be done very cautiously because of the risk of causing haemorrhage and effusion and perhaps consequent further adhesions At each session not more than one crack from the tearing of an adhesion should be obtained

Other Types of Painful Shoulder After a fall on the shoulder or after attempts to lift a heavy weight a middle aged or elderly man may develop severe pain in the shoulder region with inability to elevate the arm but with a *normal range of passive movement*. This picture can probably be attributed as a rule to the rupture partial or complete of the supraspinatus tendon There is usually tenderness over the tip of the greater *tubercle of the humerus* In a few weeks there may be gradual recovery of the power to elevate the shoulder presumably as the result of healing of the damaged tendon If there is no sign of recovery after some 6 weeks, operation may be done and the rupture sutured though there is a risk that the *frozen shoulder* syndrome may follow

Frequently patients complain of transient severe pain and sometimes partial locking during the *middle phase of elevation* although a *full range of* movement is possible This may develop after a fall or sometimes spontaneously when the onset may be very gradual The pathological basis to the trouble is probably some degenerative changes in the supraspinatus tendon It has been suggested that the symptoms are due to impingement of the outer part of this tendon where there is a tender area resulting from rupture on the under surface of the acromion process In time the symptoms usually subside often completely irrespective of treatment If the pain is severe repeated injections of procaine may be given into the subacromial region often with considerable relief If after months the shoulder remains very troublesome exploration may be *performed If a partial rupture of the supraspinatus* tendon is found it may be sutured or adhesions may be excised but it has been stated that the most effective surgical measure is removal of the acromion which gives relief of pain *without causing* disability or much change in the appearance of the shoulder

In addition to these more or less definite syndromes there are innumerable varieties and degrees of painful shoulder and as a rule it is possible only to guess at the likely pathological basis to the trouble There may be minor degrees of stiffness on examination various points of tenderness and often some weakness or wasting of the shoulder muscles If there is pain on movement procaine or steroid injections are usually worth a trial Otherwise analgesic drugs may be given The value of heat or other physiotherapeutic measures is most doubtful

Non Articular Rheumatism

Among all the conditions which are said to be rheumatic the non articular varieties are the most indefinite So little is known of aetiology and pathology that it is most difficult to give a coherent account of the matter Yet a vast number of people diagnose their own complaints as being "muscular rheumatism or fibrositis and the same diagnoses *are made very frequently* by doctors Any pain in the back or limbs and many pains in the chest and head for which there is no obvious cause are apt to be described as rheumatism Only abdominal *pains are not* labelled *in this manner* no doubt because of the existence of such diagnoses as

chronic appendicitis spastic colon and chronic dyspepsia which can conveniently be attached to them

The situation is bedevilled by the existence of speculative theories as to the pathological basis to pain of this kind and of aetiological theories to explain the hypothetical pathological changes The most popular of the pathological diagnoses is fibrositis though this is now obsolescent in medical circles The term was first employed by Sir William Gowers in 1904 He suggested that lumbago was due to hyperplastic inflammation of the fibrous tissue of insufficient degree to produce the induration or suppuration which are the manifestations of cellulitis This hyperplastic inflammation he called fibrositis Stockman in 1920 established the pathological basis of fibrositis by photomicrographs of the fibrositic nodule He observed It seems at least likely that these focal fibroses are due to small colonies of microbes invading the tissues and causing a reaction which comparatively rapidly destroys the invaders (though the microbes were never isolated) The theory of focal sepsis was also called in to explain the pathological changes of fibrositis Toxins absorbed from the teeth tonsils and other sites were thought to be transmitted to the fascii where they caused the fibrositic nodules to develop Occupational and other strains cold and damp have been alleged to be additional aetiological agents

This edifice is built on sand Much of what Gowers called fibrositis is the acute lumbago and sciatica syndrome probably due as a rule to prolapsed discs Stockman s histological observations have not been confirmed and his original slides have been re examined by other observers who have been unable to discover inflammatory changes in them The theory of focal infection has always been wildly speculative and now has been completely dropped in most circles That certain kinds of strain such as excessive and prolonged muscular effort may be followed by stiffness of the muscles and pain cannot be doubted but that is no reason to hypothesize the clinical entity fibrositis Innumerable patients claim that their limb and back pains are made worse by cold and particularly by damp but this also provides no reason for supposing that damp and cold cause pathological changes

There is evidence for supposing that some fibrositic nodules consist of tense oedematous lobules of deep fatty tissue pushed through a flaw in their fibrous covering membrane to a more superficial layer These are particularly found in the lumbar regions That such lesions occur cannot be doubted though further evidence will be needed before it can be concluded that they are responsible for widespread pain In any event these fatty herniae can hardly be related to more than a small fraction of muscular rheumatism

In recent years widespread non articular pain has been often attributed to psychoneurosis Alternatively fibrositis has been claimed to be a psychosomatic disease There is no better evidence that psychological disorders can cause pathological changes in the fibrous tissues than that cold or septic foci can do so But such disorders can undoubtedly be responsible for pain Sometimes the pain seems to be hysterical in nature—that is it is motivated for the sake of some gain derived from the pain—and sometimes it seems to be due to anxiety and depressive states In the former case there is no reason to suppose that local disturbances of any kind take place in the tissues in the latter there are possibly subtle and transient changes in the tissues caused by the emotional disorder which in turn act on the sensory nerve endings

The characteristics of psychogenic pain and the means of differentiating it from pain due to local lesions was considered on p 12 A familiar example of such pain is the widespread aching of the muscles which accompanies states of tension and anxiety in minor degree this is so common that most people have been aware of it at times A particular site of this pain is the left mammary region when it accompanies tachycardia and other cardiac manifestations of anxiety Otherwise all that need be said here is that psychogenic pain tends to be widespread persistent or continuous unrelieved by analgesics and associated with various other bodily symptoms As a rule too there is overt evidence of psychological disorder

A great deal of what has masqueraded under the diagnoses muscular rheumatism and fibrositis particularly among those who spend months away from work is this psychogenic pain But there is no justification for saying that all pain which has been called fibrositis (and is not in fact due to some such gross lesion as an osteoarthritic hip) is psychoneurotic Localized pain due to some benign and transient process can undoubtedly occur and it may be associated with stiffness and tenderness and possibly with nodules (though even when there is apparently some local basis to pain its severity is partly determined by the subject s state of mind) Injections of local anaesthetic into the tender areas may apparently cause temporary or even permanent relief of pain (This does not prove that there is necessarily some local disorder at the site of the pain Similar relief may be given when local anaesthetics are injected into tender areas due to prolapsed intervertebral discs) Pain and tenderness often accompany febrile illnesses and certain

the impression given is of an active inflammatory process In time the pain subsides and the shoulder is left stiff and painless except when movement is attempted The course of the process can thus be divided into an irritative and an adhesive stage After a further period there may be spontaneous return of movement and ultimately complete recovery may occur though probably in not more than about half the cases Some may recover partially still being left with various degrees of stiffness pain and weakness A few do not recover at all and develop gross wasting of the shoulder muscles

Treatment Shoulders which are immobilized as the result of hemiplegia and other non painful states should be regularly put through a full range of movement in the hope of preventing the freezing up process Injured shoulders should be moved to the extent which pain allows though there is the risk that movement may do further damage The attempt to move the shoulder affected by the spontaneous variety of the disorder in the acute irritative phase seems to be at best futile and at worst followed by extreme pain and an aggravation of the process Here the right course is to leave the shoulder well alone or possibly provide a sling for support and give the patient analgesic drugs Heat and other local applications are probably useless If after the acute phase has subsided there is no sign of spontaneous return of movement active steps may be considered and the same steps may be taken when the frozen shoulder has followed trauma or immobilization A simple measure is the injection of procaine into the capsule at about weekly intervals Sometimes this is followed by a gradual return of movement perhaps as the result of the self manipulation made possible by the temporary anaesthesia Injections of steroid drugs have been widely used but there have been most conflicting reports as to their value If these methods are ineffective manipulation under anaesthesia may be considered This should be done very cautiously because of the risk of causing haemorrhage and effusion and perhaps consequent further adhesions At each session not more than one crack from the tearing of an adhesion should be obtained

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bowel disease If so the diagnosis presents no difficulty

Tuberculosis This is easy to suspect if the patient is a known tuberculous subject X rays usually show a collapsed vertebra but this is not always so

Osteoporosis (*see* p 149) In elderly people and in those on steroid therapy collapse of a vertebra from osteoporosis may occur with severe pain This can be recognized radiologically

Ankylosing Spondylitis (*see* p 515) This should always be suspected in young men with low back ache Further suggestive evidence is provided by the raised E S R and minor anaemia There may be no X ray changes in the early stages Later the diagnosis is obvious

Aortic Aneurysm (*see* p 286) This causes back ache by erosion of the vertebrae which can be shown radiologically

The vast majority of backache is due to no such gross pathological states Most of it can be grouped into one of four clinical categories (1) Back pain immediately following injury (2) Backache as the evident consequence of unaccustomed use of the back muscles (3) Acute lumbago (4) Chronic low backache

Back Pain Following Injury

When back pain follows immediately upon direct injury to the back by a fall or a blow there is no aetiological problem On the other hand there may be much doubt as to the exact nature of the damage unless there is bony injury (which is revealed radiologically)

The situation is not so simple when there is no direct injury to the back but when the pain comes on with undue strain If there is a clear cut history of sudden pain developing actually while the subject is say lifting a heavy weight there can be no doubt that damage to the back has occurred—perhaps the tearing of muscle fibres or ligaments or injury to an intervertebral disc But patients habitually attribute their backache to injury without good reason In general if pain does not come on immediately upon the receipt of a blow or while actually indulging in effort but develops days or weeks later it has nothing to do with the blow or the effort And if pain develops gradually during the course of a man s usual work the strain of the work probably bears little or no responsibility for it

Backache Following Unaccustomed Use of the Back Muscles

This is very common The week end gardener for example suffers little pain actually while doing his gardening but is aware of stiffness and soreness of the lower back the following morning This gradually wears off in the course of the day and *may not prevent a further spell of gardening (with* perhaps even worse back trouble the day after) Here too the aetiology is clear though the pathology is a matter for speculation

Acute Lumbago

This is a dramatic syndrome in which there is sudden onset of severe pain across the lower back often coming on when getting out of bed or on bending or lifting Sometimes the pain is made worse by the slightest movement and is so intense that the patient is fixed in the position he happens to be and has to shout for help The erector spinae muscles may go into spasm and the back becomes rigid After some hours days or a week or two the symptoms disappear (and sometimes they can be quickly relieved by traction or manipulation) Commonly recurrent attacks of this kind occur over the course of years and are often associated with or followed by sciatica

The pathological basis to at least many examples of this syndrome is probably a prolapsed intervertebral disc particularly when there are recurrent attacks (A single attack coming out of the blue may possibly be due to say collapse of a vertebra from a secondary deposit.) Certainly the dramatic onset suggests a mechanical rather than an inflammatory process and the equally dramatic recovery which may occur spontaneously or follow traction or manipulation is further evidence for this view

Chronic Low Backache

Sometimes a patient who has had recurrent attacks of acute lumbago later develops persistent low backache with or without associated sciatica Here the probable basis of the trouble is a prolapsed intervertebral disc in most cases Much more often low backache develops insidiously particularly in middle aged women and persists indefinitely Indeed to many women such backache is apparently a normal accompaniment of middle age This is the variety of backache which should rarely be attributed to a definite pathological process though it has been wrongly attributed to a great variety of lesions such as spinal arthritis sacro iliac strain scoliosis and retroverted uterus as was noted above (p 524) Investigation is often quite fruitless and if it reveals some radiological or other abnormality it is highly doubtful whether this is related to the backache The best diagnosis to give to most patients with this kind of backache is chronic low backache

Psychological Factors Underlying Backache It may here be reiterated (*see* page 12) that the

syndromes notably 'Bornholm disease may be associated with severe localized pain (though here such labels as muscular rheumatism would not be employed) Excessive use of muscles particularly the back muscles and coughing are other factors which may be responsible for localized pain and stiffness Sometimes a process in the spine pressing on the posterior nerve roots may be the underlying lesion The common stiff neck syndrome may possibly have this basis at least in some cases

In practice pain which patients believe to be muscular rheumatism may have some gross pathological basis especially when the trouble is of recent origin It may be due to osteo arthritis of the hip joint a prolapsed intervertebral disc osseous secondary deposits tabes dorsalis obliterative arterial disease of the legs or myocardial ischaemia Care should be taken therefore to ensure that the nature and distribution of the pain does not suggest such conditions as these

Treatment Assessing the value of treatment even for disorders with a well defined pathological basis can be difficult enough assessing the value of treatment for the ill defined and variable syndromes which are called muscular rheumatism is virtually impossible Perhaps the only clear cut recommendations are that the injection of local anaesthetic into areas of persistent local tenderness is worth a trial and if the pain is severe analgesic drugs should be given The remedies which are widely used such as rubbing with embrocation pads of wool to keep the affected region warm and heat massage and other physiotherapeutic measures are all of unproven value though they possibly give symptomatic relief Iodides and sulphur (both of which were alleged to have an anti rheumatic effect) thyroid extract (unless the patient is myxoedematous) the eradication of septic foci vaccines prepared from organisms in the throat intestines or elsewhere and non specific protein therapy should be even more suspect This is not because they lack a scientific basis but because there is no evidence whatever for supposing they are effective And when they were popular they had a scientific basis Iodides were supposed to absorb fibrous tissue and eradicating septic foci or courses of vaccines were supposed to remove or neutralize the toxins causing the fibrositis

Backache

Next to headache backache is perhaps the commonest of bodily symptoms Although there are numerous definite pathological states which cause backache in a high proportion of cases its basis is obscure Because of this diagnostic difficulty the problem is often said to require the most painstaking study But this seems to imply that such study often yields fruitful results which is incorrect In fact investigating backache is in general unrewarding Moreover by painstaking study it is frequently possible to discover some abnormality and the deduction which may be quite untrue is then easily made that the abnormality is related to the symptom Abnormalities to which backache has been attributed on the slenderest grounds or no grounds include arthritis of the spine (diagnosed radiologically) scoliosis old fracture of the transverse process osteoporosis (from X ray changes of rarefaction) sacro iliac strain (from tenderness over the sacro iliac joint) faulty posture and retroverted uterus and other visceral abnormalities Fashions in diagnosing backache have greatly changed in the course of years Twenty years ago it was frequently alleged at least by gynaecologists that the commonest cause of low backache in women was retroverted uterus but backache is rarely attributed to this condition now About the same time sacro iliac strain was a common diagnosis especially by the orthopaedic surgeons now it is rarely mentioned The current popular diagnosis for backache is the prolapsed intervertebral disc Some enthusiasts have even hinted that this is responsible for the vast majority of severe backache this view is unproven and on general grounds seems unlikely

All this is not to suggest that cases of backache should never be investigated As a rule the patients who particularly require investigation are those whose backache follows immediately upon severe trauma those with a subacute and progressive story and those whose pain is dorsal (most of whom give a subacute story) Dorsal backache is comparatively rare and some gross pathological cause can often be found for it

Progressive subacute backache is likely to be due to some such serious condition as the following—

Metastatic Deposits (*see* p 531) These are by no means rare and as X rays may be normal for weeks after pain due to them has begun the condition cannot be excluded radiologically When the patient has a known growth the problem is simple otherwise metastases should be suspected when, in association with severe backache there is malaise anaemia highly elevated E S R low fever loss of weight and other general symptoms

Myelomatosis (*see* p 503) This gives a similar picture to that of metastatic deposits and it cannot be excluded radiologically It may be suspected from the blood changes Bence Jones proteose in the urine and the marrow findings

Carcinoma of Rectum It is doubtful if the primary growth is ever a direct cause of backache except in association with obvious symptoms of

CHAPTER 21

Specific and Metabolic Arthritis

A A G LEWIS and JOHN W TODD

THE vast majority of non traumatic joint disorders are of obscure aetiology and come into one of the rheumatic categories such as rheumatoid arthritis or osteo arthritis which were considered in Chapter 20 But occasionally arthritis is due to a specific infection Both the incidence and severity of this kind of arthritis has greatly lessened in recent years as the evident result of the anti bacterial drugs and the declining incidence of tuberculosis syphilis typhoid fever and some of the other infections which cause it. Joint disease is also the main feature of gout when it is related to a disturbance of uric acid metabolism

Acute Suppurative Arthritis

When pyogenic organisms reach a joint by penetrating wounds direct extension from osteo myelitis and infections of other adjoining structures or via the bloodstream from such distant infections as boils pneumonia or meningococcal meningitis acute suppurative arthritis may follow This is also an occasional complication of rheumatoid arthritis Numerous organisms including staphylococci haemolytic streptococci meningococci and pneumococci may be responsible

The condition is monarticular when due to the direct spread of infection and usually monarticular when the infection is blood borne The onset is acute with severe pain swelling and extreme tenderness of the affected joint Fever rigors headache malaise and other general symptoms also occur though they may have developed previously as the result of the causative infection The diagnosis should easily be suspected from the striking local manifestations and is confirmed by the aspiration of a purulent effusion in which the organism is demonstrated

Treatment is by the specific drug most suitable for the responsible organism If there is doubt penicillin should be given in the first instance into the joint (following daily aspiration of the purulent fluid) as well as intramuscularly As the patient is acutely ill he will naturally be in bed The affected joint will also naturally be kept still Surgical drainage which used to be common is now rarely indicated Complete recovery can usually be expected

Gonococcal Arthritis

Before the discovery of the highly-effective remedies for gonorrhoea arthritis was said to occur in some 2 per cent of cases The incidence is now much less Arthritis used to develop most often some 3 or 4 weeks after an acute infection now it is most common after mild and unrecognized attacks of gonorrhoea which have not been treated At first the arthritis often involves numerous joints and may be migratory and mild Later or sometimes initially an acute monarticular arthritis may develop usually of the knee ankle shoulder wrist or hip Sometimes there is no more than a mild synovitis with swelling and redness of the joint and minor constitutional symptoms but in other cases the process is much more severe and acute More chronic forms of arthritis often resembling rheumatoid or osteo arthritis have been said to occur but unless gonococci can be isolated from the synovial fluid—and they rarely if ever can from the chronic case—the gonococcal basis cannot be proved

The diagnosis is easily suspected when joint symptoms follow an attack of acute gonorrhoea Difficulty arises when the focus of infection in the genito urinary tract is not obvious or when its nature is obscure Isolation of the gonococcus from the primary lesion naturally leads to the suspicion that the arthritis is also gonococcal but it should not be assumed that this is necessarily so since other varieties of arthritis may develop in the subject with chronic gonorrhoea Isolation of the organism from the intra articular fluid is conclusive though the failure to do this does not exclude the condition A positive complement fixation test is good evidence of gonococcal infection but does not prove that arthritis must be gonococcal On the other hand a negative test makes the diagnosis most unlikely The failure of acute arthritis to respond to salicylates suggests but does not prove that it may be gonococcal Frequently it is impossible to be sure whether or not arthritis is gonococcal

conclusion that pain is psychogenic should be reached not by the process of excluding organic disease but from the nature of the pain the associated bodily symptoms the study of the personality and the demonstration of a relationship between the pain and the psychological state Moreover, the severity of pain which is related to an organic lesion is also determined by the psychological state some people complain bitterly of pain from a lesion which others would ignore and any individual is more pain sensitive on some occasions than on others The psychological state of patients with persistent pain should always be examined in an attempt to decide the extent to which the pain is psychologically determined Although there may well be some local process which is related to much chronic low backache psychological factors are probably important in a large proportion of cases Many of the middle aged women to whom backache is normal have numerous other complaints such as of being always tired run down and depressed and inquiry may reveal that they are constantly harassed by the problems of existence

Treatment Although it is easy to say that the treatment of backache depends on its cause this statement is of little practical help in most cases because of these diagnostic difficulties Even when backache is presumed to be due to a prolapsed intervertebral disc there is no universally applicable remedy Some patients recover without treatment and have no further trouble others have such severe pain that they need morphia others have persistent pain which can be controlled by a plaster jacket and others have such disabling symptoms as to justify operation

The treatment of backache due to ankylosing spondylitis has already been considered (p 515) There is no effective remedy for patients with backache due to myelomatosis or secondary metastatic deposits except when the primary growth is in the prostate or breast (*see* p 532) Tuberculous disease of the spine can now be treated most effectively but both this matter and the treatment of fractures and collapsed vertebrae is dealt with in surgical text books The difficult problem of the treatment of prolapsed intervertebral discs is considered elsewhere in this book (p 431) The backache which follows unaccustomed exertion hardly requires treatment

That the treatment of the common chronic low backache of obscure aetiology is unsatisfactory is evident from the vast number of patients who complain of this symptom for years in spite of trying numerous remedies A period of bed rest is said to be beneficial but even if this is so the relief is likely to be only temporary Physiotherapy particularly heat and massage is used on an enormous scale but whether it gives more than transient relief is doubtful Back strengthening exercises which are now popular have the advantage of being an active form of treatment demanding the patient's co operation and are therefore more encouraging than passive physiotherapy It may also be assumed that to improve the power and tone of the muscles is in general desirable Nevertheless there is little evidence that exercises have much effect in ameliorating backache A high proportion of women with low backache wear some kind of support This may merely be an ordinary corset but is frequently some more elaborate device made by an instrument maker Many patients claim they derive partial relief from these supports though how much this is due to their direct effect and how much to the psychological effect of wearing them it is impossible to say Manipulation and traction seem to be dramatically effective sometimes in treating patients with acute lumbago and other syndromes due to disc lesions, but their value for the subjects of chronic low backache is uncertain Finally the psychotherapeutic approach may be used The patient should be reassured as to the benign nature of the trouble whether her pain is thought to be predominantly psychogenic or predominantly organic If she had previously feared that she might be in the grip of some grave disease she may then be helped a little She should also be discouraged from believing herself to be an invalid

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urates precipitates an attack or that the excretion of urates is always diminished before one Chronic gout however is associated with hyperuricaemia and is the usual outcome of a long standing tendency to acute attacks

Clinical Picture The acute attacks are characteristic they are often precipitated by trauma stress or dietary excesses and often occur at night The big toe is usually affected the proximal joint suddenly becoming swollen red and intensely painful Within a few hours or days it becomes completely normal again Recurrences occur at decreasing intervals being associated with fever X ray changes (small round areas of erosion by urates of bone in the hands or feet) persistently raised blood uric acid and degenerative arthritis Subcutaneous deposits of urates (tophi) round these joints in bursae particularly round the elbow and in the margins of the ears give an unmistakable appearance Urate deposits in the kidneys and renal pelves may cause nephritis or renal colic

Diagnosis. This is made on the history The response of the first attack to colchicine and later the high blood uric acid X ray changes and tophi are confirmatory

Treatment In the acute attack rest and warmth are given to the joint Colchicine is prescribed 1 mg every 2 hr until relief or diarrhoea occurs A short course of ACTH or cortisone may produce dramatic relief but should be followed by colchicine otherwise another attack may occur Phenylbutazone (Butazolidine) may also be effective 1 g may be given intramuscularly or 400–600 mg by mouth in divided doses daily

In between attacks moderation in everything including alcohol should be advised A low purine diet may be helpful the simplest way to achieve this is by a vegetarian diet Salicylates have been shown to be effective in increasing uric acid excretion and in preventing acute attacks and a constant daily intake of 3–6 g (60–120 gr) in divided doses should be maintained for three months or more then reducing to this dosage on three or four days of the week Probenecid (Benemid) has a similar action to salicylate and can be given in four daily doses of 0 5 g Both drugs inhibit the tubular reabsorption of urate this effect is enhanced by sodium bicarbonate which also prevents renal colic from uricosuria and reduces the gastric irritation and high blood level of salicylate resulting from continuous administration The patient should be instructed to take up to 10 g (150 gr) daily to keep the urine alkaline to litmus

In chronic gout some benefit may be derived from a low purine diet One of the above drugs should be given to increase uric acid excretion when many of the tophi and other urate deposits may be slowly absorbed

The most important therapeutic measure is the eradication of the primary infection by penicillin. This may be followed by resolution of the joint condition especially when this is acute. When the arthritis is chronic it may persist in spite of penicillin though there will then be doubt as to whether it is gonococcal. Local measures applied to the affected joint probably have little effect.

Meningococcal Arthritis

Occasionally acute suppurative arthritis of a single joint occurs as a complication of meningococcal meningitis usually about a week after the onset; this has already been mentioned above (p. 527). A transient polyarthritis usually concurrent with the meningeal signs is more common. In both these circumstances there is no diagnostic problem.

Meningococcal septicaemia sometimes occurs without meningitis but presents with joint symptoms and fever and often with an associated skin eruption. The joint symptoms are variable. There may be polyarthritis with pain, redness and swelling which sometimes flits from joint to joint, suggesting rheumatic fever, or alternatively a monarticular serous or purulent effusion. The skin eruption is variable both in extent and nature and may be purpuric, macular or maculo papular. If arthritis occurs alone the condition is likely to be overlooked, but an associated skin eruption should arouse suspicion. The diagnosis is confirmed by isolating meningococci from a blood culture. Treatment is by penicillin or sulphonamide or both and is similar to that of meningococcal meningitis (p. 392).

The Arthritis of Scarlet Fever

Some 2 per cent of patients with scarlet fever have joint involvement. The most common type is a transient polyarthritis about a week after the onset which subsides in a few days and leaves no cardiac or other sequelae. More rarely rheumatic fever develops 3 or 4 weeks after the onset of the sore throat. More rarely still there is acute suppurative arthritis of a single joint due to haemolytic streptococci.

The Arthritis of Bacillary Dysentery

About 1 per cent of patients with bacillary dysentery develop arthritis either at the same time as the dysentery or up to several months later. There is an acute arthritis of one of the larger joints or sometimes a polyarticular affection of the small hand or foot joints with much synovial effusion. The nature of the process is obscure since the dysenteric organisms can rarely if ever be isolated from the synovial fluid. The arthritis usually clears up after some weeks or months without sequelae. It is doubtful whether treating the dysentery by sulphonamides has any effect on the course of the joint process.

The arthritis which may accompany ulcerative colitis seems to be of a similar nature.

Syphilitic Arthritis

Widespread joint pains and occasionally synovitis with effusion affecting one or several of the larger joints may be a feature of secondary syphilis. In the tertiary stage there are rarely painless hydrarthroses. When these occur in children with congenital syphilis they are known as Clutton's joints; the knees are most often affected. The underlying lesion is probably a miliary gummatous synovitis. In other patients there are gummatous deposits in the bone or cartilage, with consquent destruction of the joint structures. The treatment is that for other forms of syphilis.

Tuberculous Arthritis

In common with other varieties of tuberculosis tuberculous arthritis becomes more rare as the years go by. It chiefly affects children and young adults and is secondary to a primary focus elsewhere. The condition is usually monarticular and the spinal joints are most often involved, followed by the knee, hip, elbow, ankle and wrist. The onset is insidious with stiffness and pain in the affected joint and later there may develop the characteristic 'doughy swelling' and much muscular wasting. Unless the patient is known to have tuberculosis the diagnosis in the early stages is difficult. The prognosis has been greatly improved by the modern drug treatment of tuberculosis. Since the condition is considered to be a surgical problem no more will be said of it here.

Gout

Gout is a disease characterized by paroxysms of extremely painful arthritis with a tendency to a high blood level of uric acid, local deposition of urates and eventually a chronic disabling arthritis. It is much commoner in males, usually appearing in the thirties; in women it occurs only after the menopause. There is a strong familial tendency.

Uric acid is derived from the metabolism of purines, the normal upper limits being 4.5 mg/100 ml in blood or 6 mg/100 ml in serum. The exact relationship between the rates of urate formation and deposition and the acute attack is unknown. There is no conclusive evidence that purine or protein metabolism is increased in gout, that a general or local rise of the blood or tissue concentration of

when found in the obscurely ill patient A persistently increased formol stable acid phosphatase figure (upper limit of normal 5 units) is virtually diagnostic of osseous secondary deposits due to prostatic carcinoma

A markedly raised blood calcium figure accompanies hyperparathyroidism and a low figure hypoparathyroidism A low figure may also be due to rickets osteomalacia chronic nephritis obstructive jaundice and other diseases

The E.S R is elevated in the presence of many extensive bone diseases and is often associated with anaemia These findings are of little importance either in pointing to a diagnosis or in assessing the severity of the process

Osteitis Deformans (Paget s Disease of Bone)

A chronic affection of one or many bones but not of the whole skeleton causing softening enlargement and deformity Lesions are found somewhere in about 3 per cent of routine autopsies in persons over 40 It is usually first discovered in the sixth decade and is very rarely discovered below the age of 40 It is probably a little commoner in men than in women and tends to run in families Its cause is unknown

Pathology The most frequently involved bones initially are the lumbar vertebrae and sacrum skull pelvic bones other than the sacrum tibia femur and clavicle probably in that order Ultimately any bone may be affected Sometimes the process is confined to one bone for long periods and in about 10 per cent of cases permanently The essential process seems to be localized bone resorption accompanied by the rapid deposition of excessive amounts of irregular new bone some of which does not become fully calcified but remains in its osteoid form This new bone formation is most pronounced beneath the periosteum and is thicker coarser spongier and more vascular than normal bone The serum alkaline phosphatase figure is elevated—even to 20 times the normal where the process is active The serum calcium and phosphorus levels are unaltered or only slightly increased

Clinical Picture The disease causes no symptoms throughout life in most cases Frequently it is discovered by accident during radiological examination for other conditions When a patient has such symptoms as headache or backache and is found to have osteitis deformans it should not be assumed that the symptoms are necessarily due to the bony disorder Progressive enlargement of the skull bowing and thickening of the tibiae or femora or kyphosis are often the first complaints In advanced cases there may be an enormous head with extreme kyphosis a pendulous belly and shortened deformed legs Pain apparently due to the bone condition is sometimes severe and persistent and there is occasionally pain from compression of the nerve roots Paraplegia from spinal cord involvement or blindness or deafness from compression of the cranial nerves are rare complications The skin overlying the affected bone may be warm owing to the increased vascularity of the bone In advanced cases this may be followed by circulatory changes similar to those accompanying an arterio venous shunt and leading to cardiac failure Spontaneous fractures which usually unite well are fairly common Sarcoma of bone is a rare complication of the disease when it has been present for many years

The X ray picture is fairly characteristic There is widening of the cortex with irregular areas of thickening and decalcification the appearance suggesting that of cotton wool especially in the skull The long bones may be obviously bowed

Diagnosis The typical advanced case is obvious Otherwise the X ray appearances are usually sufficiently characteristic to leave little doubt as to the diagnosis Occasionally there is difficulty in differentiating osteitis deformans from carcinomatosis Time soon solves the problem since carcinomatosis is a rapidly progressive condition accompanied by severe constitutional symptoms but with slight or moderate elevation in the alkaline phosphatase level (though there is a marked rise in the acid phosphatase if the primary growth is prostatic)

Treatment No remedy has any proven effect on the course of the disease Calcium and vitamin D have been given on theoretical grounds and claims have been made that testosterone and stilboestrol are beneficial The most important remedy is analgesic drugs Radio therapy is also possibly effective in relieving pain Supports may be of help when there is great deformity The disease can be distressing to the patient from the skull enlargement and the deformities and he should be reassured as to its comparatively benign nature

Metastatic Lesions of Bone

Nearly all types of carcinoma sometimes give rise to secondary deposits in bone When the patient is known to have had a malignant growth it is easy to suspect (though not always so easy to prove) that widespread pain may be due to such deposits Not infrequently osseous secondary deposits cause the first symptom of a malignant growth The diagnosis then may be difficult and this difficulty provides the justification for this section

The primary growths which most often give rise to osseous secondary deposits are probably those

CHAPTER 22

Diseases of Bone

JOHN W TODD

BONE consists mainly of calcium and phosphate deposited in a matrix of collagenous fibrils Deposition of bone by osteoblasts and absorption by osteoclasts continue throughout life The osteoblasts lay down the matrix which normally calcifies immediately The osteoclasts are *multi nucleated* giant cells Osteoblastic activity is associated with the liberation of the enzyme alkaline phosphatase (an increased amount of which accompanies many diseases of bone)

Bone development is dependent on numerous factors The most important of these probably are

1 An adequate supply of calcium and phosphorus in the food

2 Satisfactory absorption of calcium and phosphorus from the intestine This absorption may be hindered by lack of vitamin D and by chronic disorders of the small intestine such as gastro colic fistula and the sprue syndromes

3 General bodily activity Activity increases bone formation inactivity from prolonged rest in bed is associated with decalcification of bones

4 The parathyroid glands Excess of parathyroid hormone causes increased excretion of calcium and phosphorus with decalcification and is accompanied by a rise in the blood calcium content Deficiency of the hormone causes the reverse changes and is characterized by tetany due to a low blood calcium level

5 Other endocrine glands Hyperthyroidism may be accompanied by increased excretion of calcium and some decalcification Cushing s syndrome (from hyperplasia of the suprarenal cortex) is accompanied by osteoporosis

6 Adequate renal function Adolescents with chronic pyelonephritis or hydronephrosis may have decalcification of bones and often retarded growth —the so called renal rickets

In practice bone disorders due to abnormalities of these factors are rare Many of them are considered elsewhere in this book under the deficiency states (such as rickets and osteomalacia) the endocrine disorders or diseases of the kidneys Much more often bone disorders are of obscure aetiology or are due to various infections

Many bone diseases are said to be surgical and therefore have no place in this book These include osteomyelitis—an infection of bone usually due to the *Staph aureus*—tuberculosis of bone fractures and primary tumours such as osteogenic sarcoma and osteoclastoma

Bone is frequently involved by the spread of diseases arising elsewhere Osteomyelitis may be secondary to a boil carbuncle or other staphylococcal infection Tuberculosis of bone may complicate pulmonary or genito urinary tuberculosis Metastatic malignant disease including leukaemia frequently involves bone and sarcoidosis does so occasionally Aortic aneurysm may directly erode the vertebrae and malignant tumours may directly invade bone All severe joint disorders more or less affect the adjoining bone These conditions with the exception of metastatic malignant deposits will not be further considered here as they are dealt with under the appropriate disease processes Myelomatosis is a disease of marrow rather than of bone itself and is included in the haemopoietic disorders (p 503)

Investigations X rays are of prime importance in investigating bone diseases Sometimes the X ray appearances are virtually diagnostic and frequently they are suggestive Sooner or later there are X ray changes due to most diseases involving bone though sometimes these do not develop until symptoms have been present for a long time

The estimation of phosphatase activity may shed considerable light An alkaline phosphatase figure definitely increased beyond the upper normal limit of 13 units may be associated with many bone diseases including Paget s disease hyperparathyroidism and metastatic deposits But a similar high value is also a feature of obstructive jaundice and occasionaly accompanies other disorders In none of these conditions moreover is the alkaline phosphatase figure invariably elevated This estimation therefore is of little diagnostic value though by drawing attention to the likelihood of some general disease of bone an increased figure is very useful

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arising from the lung breast prostate and kidney both because these growths are common and because they frequently metastasize in bone rather than in other places Growths arising in the thyroid, alimentary tract ovary testicle and bladder also metastasize in bone sometimes though thyroid and testicular growths are both rare Presenting symptoms due to osseous secondary deposits are particularly common when the primary growth is in the lung and there may then be no or few symptoms from the lung itself

The mode of spread of the growth is usually by the blood stream though occasionally by the lymphatics or by direct invasion (especially from lung growths) The bones most often affected are the vertebrae pelvis ribs skull femur and humerus the bones least often affected are those of the legs feet forearm and hands Most secondaries cause absorption of bone but some cause a combination of absorption and deposition Occasionally the predominant process is deposition especially when the primary growth is prostatic The deposits are usually multiple but not rarely are single

Clinical Picture The first manifestation of a long bone metastasis may be a spontaneous fracture with little preceding pain or other symptoms Other long bone deposits are responsible for persistent and severe localized pain without radiological changes at first though these usually develop in a few weeks Vertebral deposits are particularly likely to lead to diagnostic errors because their presenting symptom is pain in the back (which may be widespread or in the area of distribution of one or more nerve roots) and backache is such a common symptom that it is apt to be disregarded Moreover clinical examination may reveal no convincing signs and X rays are as a rule normal for many weeks or sometimes months after the pain develops Rapidly developing paraplegia is a by no means rare manifestation of a vertebral deposit The symptoms of rib deposits may easily be misinterpreted as ' intercostal neuralgia or pleurodynia When there are multiple small deposits in the bones of the thoracic cage or pelvis the symptoms of anaemia are sometimes the presenting feature with little accompanying pain When this anaemia is of the leuco-erythroblastic type with nucleated red cells and a moderate leucocytosis some of the leucocytes being immature forms there should be a strong suspicion of osseous metastases

It may be at first impossible to confirm that such symptoms as these are due to malignant metastases though sometimes clinical or radiological study of the likely sites of a primary growth will reveal suggestive findings The problem is naturally simpler when the primary is in the breast thyroid, or other superficial organ than when it is in the lung or other deep situation In particular, a normal chest X ray does not exclude a primary lung growth though most lung growths cause some abnormal shadowing in the X ray Certain non specific investigations including a greatly elevated E S R and elevated alkaline phosphatase level may give additional grounds for suspecting metastatic deposits A marked rise in the acid phosphatase level strongly favours the diagnosis of osseous deposits from a carcinoma of the prostate

In spite of all efforts the situation may remain obscure until radiological or other evidence suggesting malignant disease develops perhaps weeks or months later The first radiological change due to destructive or osteoclastic deposits are usually single or multiple translucent areas though sometimes generalized osteoporosis occurs Osteoblastic deposits cause scattered irregular opacities which may later coalesce so that the whole bone appears dense

Treatment When the deposits are from carcinoma of the prostate stilboestrol in doses of about 10–30 mg daily should be given indefinitely This often causes complete disappearances of symptoms for years Deposits from carcinoma of the breast may also be made to retrogress for a time by female sex hormone in post menopausal cases and male sex hormone in pre menopausal cases though the results are generally far inferior to those with prostatic growths If hormone treatment fails oophorectomy with or without adrenalectomy and hypophysectomy may all be followed by temporary retrogression of deposits from breast cancer Otherwise the outlook is extremely bad and nothing can be done beyond giving analgesics or possibly radiotherapy which may give temporary relief

Hypertrophic Pulmonary Osteo-arthropathy

A symmetrical enlargement of the bones and soft tissues of the extremities

Aetiology In some 90 per cent of cases the disorder follows certain chronic diseases usually intrathoracic The most common are carcinoma of bronchus bronchiectasis chronic empyema chronic lung abscess and pulmonary tuberculosis among lung conditions and congenital heart disease and infective endocarditis (especially when associated) among heart conditions Less common diseases are acquired heart disease aortic aneurysm, pyonephrosis cirrhosis of the liver chronic jejuno ileal insufficiency ulcerative colitis and polycythaemia In the remaining 10 per cent of cases no evidence of associated disease can be found though in some of these the condition is hereditary

Why patients with such conditions develop hypertrophic pulmonary osteo arthropathy is not known

Why one individual with say carcinoma of bronchus should rapidly develop the disorder whereas another with apparently similar lung disease does not is equally obscure

Pathology There is thickening and hyperaemia of the soft tissues of the hands and feet with some enlargement of the bones particularly the phalanges Later periosteal thickening may develop which can be seen radiologically and finally there may be new bone formation The process may affect all the phalanges except the terminal which usually escape the wrists and ankles and the shafts of the arm and leg bones

Clinical Picture The condition may advance *pari passu* with the underlying disease but sometimes long precedes the symptoms due to this disease and therefore leads to its discovery As a rule the onset is gradual though when accompanying carcinoma of bronchus it is sometimes quite rapid The first and most common feature is clubbing of the fingers Similar clubbing of the toes also occurs but is less striking as a rule The nails become markedly curved and the finger ends are unusually warm Later painless enlargement of the hands forearms feet and legs may develop Alternatively there may be painful and swollen finger or toe joints suggesting the picture of rheumatoid arthritis and the wrist ankle elbow and knee joints may ultimately be affected There is sometimes considerable oedema

The course of the condition depends on the underlying disease In so far as this can be ameliorated the hypertrophic pulmonary osteo arthropathy will resolve After pneumonectomy for carcinoma of the lung improvement may occur within hours Otherwise there is no effective remedy

Congenital Bone Disorders

Congenital abnormalities of bones are all fairly rare and many varieties are so very rare that only occasional examples have been described Many are familial The following are the least uncommon and most-easily recognized types

Achondroplasia

This is a hereditary disease and is transmitted equally to both sexes as a mendelian dominant Half the children of affected parents are themselves affected Sporadic cases resulting from mutations occur once in every 10 000 of the population The chances of normal parents who have already had one achondroplasic child having another remains 1 in 10 000 Because of the high still birth rate and infantile death rate (80 per cent die in the first year) and no doubt because many adult achondroplasics never marry the disease in any family soon dies out it is rarely seen in more than two generations

The essential disorder is faulty development of bone derived from cartilage beginning in intra uterine life The usually affected bones are the femur tibia radius ulna pelvis base of skull foot and hand bones vertebrae and ribs in that order of frequency The epiphysis may be normal in size or hypertrophied but the shafts of the bones are short and thick The condition is obvious at birth the child being a dwarf with short limbs and relatively large head If death does not occur in the first year the expectation of life is not much diminished The adult achondroplasic is usually less than 55 inches in height with a trunk not much below average size but with very short thick and bowed limbs a large skull but small face prominent lips and jaws and a depressed nose The fingers are nearly equal in length and are short and fat and there is lumbar lordosis and a contracted and tilted pelvis The unfortunate individual is so striking as to be recognizable from a long distance Mental and sexual development are usually normal There is no treatment

Osteogenesis Imperfecta (Fragilitas Ossium)

This is a rare congenital disorder in which there is abnormal fragility of the bones with consequent fractures Frequently several members of a family are affected though sporadic cases occur Associated abnormalities are blue sclerotics due to the pigmented choroidal layer being visible through the sclerotics and otosclerosis though this does not develop until adult life The relatives of those with the disease whose bones appear normal often have blue sclerotics There are no characteristic biochemical changes though there may be inconstant elevation in the alkaline phosphatase level The most severe cases develop before birth and the infants are still born or soon die with multiple fractures and deformities Less severe cases seem normal at birth but fractures occur when the infant begins to crawl or walk The mildest cases do not develop fractures until adolescence or later There is a natural tendency to improvement as the years go by and if the subject survives to adult life he may thereafter have few or no more fractures When fractures are numerous deformities result which may be gross The radiological appearances are of osteoporosis with slender long bones The picture is so striking that there can hardly be diagnostic confusion No treatment affects the course of the process though deformities from

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CHAPTER 23

Disorders Due to Physical Agents

CHARLES A ST HILL

The Effect of Temperature Changes on the Body

Cold

EXPOSURE of the body to low temperatures may produce local tissue damage such as frostbite trench foot and chilblains or a generalized lowering of body temperature with a risk of death due to hypothermia

Generalized Hypothermia

When the body is exposed to cold it protects itself by reducing heat loss by means of a reduced blood flow through the surface capillaries and increases heat production mainly by the process of shivering Unless the outside temperature is very low this is sufficient to keep the temperature of the inside of the body (as judged by the rectal temperature) at about normal level If the cold is intense the internal body temperature starts to fall In the early phases this is accompanied by intensified shivering but when the rectal temperature falls to about 88 to 90 F the persistent shivering passes off and is replaced by generalized muscular rigidity interrupted by occasional shivering bouts At this stage the patient becomes quiet and his consciousness clouded The fall in body temperature is accompanied by a marked reduction in metabolic rate with lowered oxygen consumption and a fall in heart rate and blood pressure If the hypothermia persists a considerable reduction in blood volume occurs As the body temperature continues to fall cardiac arrhythmias occur due to the effects of the body s lowered temperature on the pacemaker These irregularities increase in severity and are usually the cause of death

Treatment The object of treatment must be to return the body temperature to normal Drugs are of no value In fact any drug or stimulant such as brandy causes cutaneous vasodilatation which may do harm by increasing heat loss through the superficial circulation The only way to assist the patient s own heat producing metabolism is by applying warmth Two dangers must be borne in mind when this is contemplated First if the skin is moderately warmed vasodilation of skin vessels will be produced and a large volume of blood will flow through severely-chilled tissues This will cause a further fall of the internal body temperature which may prove disastrous Secondly if over-cooling has been present for a long time and the blood volume consequently reduced a sudden dilatation of superficial vessels by the application of considerable warmth may produce a dangerous fall in blood pressure It is probable therefore that after short periods of hypothermia the patient should be treated by immersion in a really hot bath This will not only dilate superficial vessels but heat the superficial tissues so that the inevitable initial fall in internal body temperature will be minimized If the exposure to cold has been protracted the patient should be transferred to a slightly warmed room (about 70 F) and allowed to warm up very slowly

Local Hypothermia

Trench foot or immersion foot Prolonged exposure of the limbs to damp cold in the presence of a degree of cooling of the rest of the body leads to damage to the limbs so exposed

The damage is probably due to generalized arterial spasm of the limb vessels coupled with areas of venous and capillary over dilatation with pooling of blood This condition is seen in soldiers standing for long periods in cold waterlogged trenches and in ships crews who have had their legs immersed in cold water in open boats or on rafts

When first seen the feet and lower parts of the legs are white and numb and walking is difficult because of lack of sensation After a few hours warmth the affected parts become hot and swollen and give rise to severe burning pain Later blistering and patchy gangrene may appear Recovery

fractures can to some extent be prevented by suit able splintage

Marble bone Disease (Osteopetrosis)

This very rare condition may be discovered at any age though it probably exists from birth The affected bones are hard and dense The extent of the process varies greatly The milder cases are dis covered by accident through radiography which shows symmetrical sclerosis of the long bones be ginning at the extremities and extending to the middle of the shafts Later there may be obliteration of the marrow cavity More severe cases may come to light as the result of fractures or if the base of the skull is affected there may be cranial nerve palsies or hydrocephalus The marrow involvement sometimes leads to leucoerythroblastic anaemia or ultimately aplastic anaemia There is no treatment

Oxycephaly

This is a form of head deformity due to prema ture union of the cranial sutures and is sometimes familial The skull is short high and domed and the brow ridges are poorly developed the patient having a most striking appearance The shallowness of the orbits causes exopthalmos This may be so extreme as to be accompanied by divergent squint, visual loss or severe ulceration which may necessi tate removal of the eyes The intracranial pressure may be raised with resultant headache vomiting and papilloedema A high narrow hard palate is common There is sometimes mental defect. Apart from orbital decompression for the exophthalmos there is no effective treatment

sweating In very hot climates many litres of sweat may be produced leading to a very high daily sodium chloride and water loss The human body can recognize water deficiency as thirst but does not appreciate salt deficiency The sufferer therefore attempts to make good his water loss by drinking large quantities of water but because of the electrolyte deficiency of his blood stream this is largely lost again through the kidneys The dehydration therefore steadily worsens If the sodium chloride deficiency becomes grave the patient may experience crippling muscular cramps particularly affecting muscles subjected to hard work Alternatively the cramps may be initiated by drinking large volumes of water which on absorption dilute the already depleted blood electrolytes still further If the condition is not remedied gross dehydration with vomiting lassitude loss of weight dry inelastic skin and suppression of urine may progress until death occurs

Treatment This consists in replacing both the lost water and sodium chloride which may be done by the addition of ¼ to ½ per cent salt to drinking water If vomiting has started the deficiency may have to be made good by intravenous infusion of physiological saline If this severe stage has in fact been reached it should be remembered that the patient may lack 30 to 40 g of salt and 4 or 5 l of water

Changes in Atmospheric Pressure

Lowered Atmospheric Pressure

At high altitudes the partial pressure of the oxygen in the atmosphere is considerably decreased The effects of this on the human body depend upon the rapidity of ascent to high altitudes (and therefore low oxygen tension) and the age and physique of the subject Young adults up to the age of 25 years adapt themselves best, but most individuals feel some effects if a rapid ascent is made to above 10 000 ft above sea level and a height of about 24 000 ft above sea level is the limit to which man can ascend without prolonged preliminary training

If the ascent to high altitudes is rapid sudden loss of consciousness may occur but if the ascent is slower whether it be by plane or in the course of climbing a mountain the symptoms of so-called mountain sickness make their appearance The first to be experienced is a feeling of exhilaration and excitement As higher altitudes are reached this gives way to a sense of weakness with dyspnoea cyanosis headache and vomiting At the same time mental acuity becomes decreased and the person affected may embark on dangerous ill judged actions without consideration of the risks involved Personality changes also take place normally good humoured easy going companions becoming morose irritable and quarrelsome If the altitude is still further increased complete prostration may supervene and death follow in a matter of time If some weeks are spent at an increased altitude the development of acclimitization (which includes an increase of the red blood count to a polycythaemic level) produces a disappearance of symptoms

Caisson Disease

If the atmospheric pressure to which an individual is exposed is decreased with extreme rapidity symptoms quite different from those of mountain sickness may appear The decrease in pressure causes nitrogen which had previously been kept in solution by atmospheric pressure to evolve in gaseous form The bubbles of gas so liberated in the blood stream and tissues are responsible for the symptoms and signs This phenomenon tends to occur in divers who are too rapidly raised from deep dives where air has to be delivered to them under considerable pressure and in air crews and passengers travelling in pressurized aircraft cabins if a leak occurs and the cabin pressure is suddenly reduced Because of the prevalence of this condition among divers it has been given the name Caisson Disease or Divers Bends The earlier symptoms take the form of cutaneous sensations of itching and patchy feelings of cold or warmth This is followed by severe pain in the joints particularly the knees together with evidence of central nervous system involvement such as vertigo and sometimes epileptiform attacks or paraplegia Death may occur in severe cases from central nervous system involvement or from cardio-respiratory embarrassment if the liberation of gas into the circulation becomes excessive

Treatment. This consists in rapid recompression of the atmosphere to its former level followed by very slow decompression In aircraft the recompression may be brought about by rapid descent to low altitudes

If the condition occurs in divers they must be transferred to special depots where apparatus is available for recompression of the atmosphere to its former high level

from this stage frequently leads to continuing anaesthesia atrophy of small muscles and anhydrosis which may last for months

Frostbite The application of very severe cold (e g an arctic wind) to a small isolated exposed part of the body produces damage akin to that seen in trench foot but known as frostbite This condition usually affects the nose face ears fingers or toes The affected area appears as a white patch standing out in sharp contrast to the surrounding skin and feels hard and cold to the touch If warmed such an area becomes hot red and oedematous with a sensation of burning pain If the frost bitten area is allowed to remain for more than about half an hour blistering and gangrene may occur when warmth returns

The mechanism of frostbite is probably a local arterial spasm with paralytic capillary damage similar to that of trench foot In addition the direct action of cold on the tissues themselves may play a part in the process

Treatment Considerable argument exists as to the best method of treatment of trench foot and frostbite The majority view is that very slow warming of the parts concerned results in the least risk of damage when the circulation is restored Because of the liability of blistering and gangrene friction by rubbing or massage must be avoided and steps should be taken to cut down infection should tissue breakdown occur

Chilblains

These common painful and irritating lesions are liable to occur in wet cold climates but are rarely seen in drier climates although the temperature may be consistently very low They take the form of slightly raised tender red patches on the feet hands and sometimes the nose and ears which itch intensely when the part is warmed If the condition persists the surface skin may blister and ulcerate They seem to be due to local areas of arteriolar spasm coupled with capillary dilatation and stasis

Treatment Treatment of these tiresome lesions is unsatisfactory Success has been claimed by medication with high doses of various vitamins vasodilatatory drugs and calcium together with the local application of various compounds None of these treatments has produced consistent success although individual cases may benefit

Heat

The local effects of the application of excessive heat to tissues such as burning and scalding are not within the scope of this book The effects of generalized overheating of the body warrant discussion however The most serious results of overheating take the form of heat stroke and heat exhaustion In addition irritation of the skin may be produced by prolonged exposure to very hot atmospheres and may cause considerable discomfort

Heat Stroke (Sunstroke)

This condition was at one time thought to be due to the action of the sun s rays upon the head or neck It is now accepted that it is due to a breakdown of the heat regulating centres of the brain under the stress of excessively hot atmospheric conditions The syndrome is most liable to occur in non acclimatized people particularly if elderly and arteriosclerotic and least in acclimatized fit young adults

The onset is sudden the patient complains of headache malaise giddiness and nausea and may vomit These early symptoms are rapidly followed by collapse and coma The body temperature rises to 106°F or above temperatures of 110 F or even higher having been recorded Death supervenes in a matter of hours if treatment cannot be instituted since the central nervous system rapidly undergoes irreversible damage at these temperatures

Treatment This consists in cooling the patient Cold baths or ice packs have been recommended so that the body temperature may be reduced as rapidly as possible from the dangerously high level to which it has risen In the absence of these methods of cooling every effort should be made to transfer the patient to a cooler place and to reduce the temperature by cold water sponging Antipyretic drugs are valueless

Heat Exhaustion

Anybody who attempts to indulge in too active an existence in excessively hot climates may suffer from exhaustion due to the heat It is more liable to occur in the unacclimatized particularly in the unfit and older age groups The symptoms are variable and include irritability fatigue dizziness palpitations nausea and headaches They are aggravated by exercise and may lead to collapse and even unconsciousness The temperature may be somewhat raised but does not reach the levels attained in true heat stroke and if the patient rests in a cool place recovery soon takes place

True Heat Exhaustion is produced by a progressive water and salt deficiency due to excessive

the examining doctor to elicit evidence of heart beat respiration or consciousness should not be taken as evidence that death has in fact taken place Treatment should begin forthwith and be carried on for a long time a number of cases of recovery having been reported after apparently unsuccessful treatment had been maintained for many hours

Treatment. Treatment of the unconscious pulse less patient should begin without an instant s delay since the central nervous system can tolerate only a few minutes anoxia from circulatory deficiency before irreversible changes occur Artificial respiration must be instituted as this not only maintains ventilation of the lungs but promotes a certain degree of cerebral circulation which may be sufficient to maintain the viability of the central nervous system The efficiency of the various methods of artificial respiration in promoting circulation varies Sylvester s method is probably best but there is no general agreement on this point. Whichever method is utilized should be continued without cessation until all hope of recovery is passed It is a difficult matter to decide when to give up hope and because of this and the reports of recovery after very long periods of treatment it has been suggested that artificial respiration should be continued until incontrovertible proof of death is afforded by the onset of rigor mortis

A number of methods have been suggested for the initiation of normal cardiac action The simplest of these is the application of rapid indirect percussions to the heart by a series of rapid slaps to the abdomen just below the xiphisternum Intracardiac injections of adenosine triphosphate have been shown experimentally to convert the fibrillating heart of the electrocuted dog to normal rhythm Finally even direct cardiac massage has been recommended These last two methods of course need special drugs or equipment which are not often available at the time of the accident, so that prolonged artificial respiration is the backbone of treatment.

Treatment of burned and disrupted tissue should follow the usual lines The extent of deep tissue destruction may be very great even in the presence of only minor skin damage The destruction of tissue may be so great that renal damage allied to that produced by the crush syndrome or transfusion reactions may occur with oliguria albuminuria haematuria and uraemia. Treatment of this should conform to the lines indicated for lower nephron necrosis (*see* Mercury Poisoning page 548)

Radiation Injury

The rapid expansion of the manufacture of radioactive substances their use in industry and medicine together with the development of atomic missiles has increased the potential dangers of disease due to radioactive emanations The active agents responsible for the effects of radiation are X rays gamma rays fast and slow neutrons and beta and alpha particles These may affect the body by being projected into it from without (as in X ray therapy) or by the introduction of radioactive isotopes into the body by accident or design

The clinical manifestations of exposure to radioactive emanations depend upon the area of the body exposed the length of exposure and the dose of radiation Under normal every-day conditions the population of the world is subjected to a very small degree of radioactivity from the atmosphere and the repeated detonation of atomic devices has raised the possibility of an increase in intensity of this It seems however that the daily exposure to radio activity to which we are all subjected will remain very far below the 0 3 roentgens per week that has been suggested as the dose above which damage may be done to the body if continued over a period of years Workers in X ray Departments and in the production of radioactive substances are at constant risk of chronic overdosage and in the event of a major war entire populations may be in danger of sudden enormous over-exposure

Chronic Exposure to Small Doses of Radioactive Substances If the radiation is of external origin it may produce local or general effects depending upon whether the whole or partial exposure of the body occurs If the radiation is confined to one part of the body the skin of the area affected may become atrophic and dry and small cuts and abrasions will heal only with difficulty If exposure continues painful ulcerations may appear and these may be of malignant epitheliomatous nature If exposure is more general its effects are most marked in the eyes producing lens opacities the genital organs causing sterility and on the haemopoietic system resulting in a slowly progressive aplastic anaemia or sometimes leukaemia

The absorption of radioactive substances into the body over a long period of time produces effects mainly in the bone marrow resulting in thrombocytopenia agranulocytosis or a full aplastic anaemia with all the signs and symptoms associated with these conditions Lesser doses may produce

Motion Sickness (Sea, Air and Car Sickness)

The subjection of the human body for prolonged periods to unaccustomed movement through space may initiate the reception of such severe stimuli by the *semicircular canals and secondary* areas connected with balance that unpleasant and dis abling symptoms may occur There is a marked individual variation of susceptibility to these stimuli some people being unaffected by the heavy rolling of a ship *for hours or days others becoming ill* after a few minutes travel in a car In addition the type of motion to which the body is subjected plays a part in individual sensitivity Thus an up and down motion may particularly affect one individual while *another is upset especially by changes in* velocity on a horizontal plane

The symptoms of motion sickness may appear abruptly or gradually The victim becomes de pressed and apprehensive Salivation is excessive and is accompanied by nausea *followed by vomit* ing which continues although the stomach is empty The sufferer is pale and sweating and may have considerable mental depression The symptoms con tinue until the unaccustomed motion ceases or until the patient becomes acclimatized a *process* that may take two or three days Acclimatization of the balance centres is by no means permanent and many a seafaring man (*e g* Nelson) has the repeated bitter experience of sea *sickness during his first few* days at sea after every leave Past memories of motion sickness and the anxiety caused by won dering whether the experience will be repeated all play their part in making the condition more likely

Treatment Many *remedies* have been *suggested* and in certain individuals may be successful These include blocking the ears with plugs of cotton wool generous medication with whisky gin or other specified alcoholic beverage or in the case of car sickness trailing a chain from the axle of a car so as to earth static electricity The efficacy of these types of remedies probably lies mainly in suggestion *or as in the case of alcohol* in removing anxiety Certain drugs are now widely used with general benefit for motion sickness sufferers These drugs act by depressing the parasympathetic nervous sys tem The earliest to be used was hyoscine in 0 5 to *1 mg doses and there can be no doubt that during* the last war many soldiers on landing craft were protected from seasickness in this way Since that time numerous compounds known under such trade names as Dramamine Avomine etc have been introduced *which seem to* have a good sup-pressive action on motion sickness and have minimal side reaction These drugs should be administered about half to one hour before beginning to travel

Electric Shock

The effects of the passage of an electric current through the body are variable Muscular convul sions cessation of cardiac action and respiration local tissue destruction and loss of consciousness *are all liable to occur but one or more of these* manifestations may predominate markedly over the rest In general it may be considered that the vic tim of low voltage (less than 500 volts) electric shocks will be unconscious pulseless and apnoeic but show little evidence of burning whereas the victim of high voltage shocks may undergo only the most transitory loss of consciousness but suffer very severe *local tissue burning and destruction in the* region of the site of entry of the current The ex planation for this probably lies in the fact that when the victim makes contact with an electrical source of high voltage an enormous surge of energy passes *from* the point of contact throughout the whole body This causes destruction of tissue around the point of contact and spreading through the body sends the whole *musculature into spasm* The violent contraction of the back muscles hurls the victim backwards and tears him from his contact By this means his central nervous system and the conductive tissues of the heart are subjected to the *electrical current for only a fraction of a second* too short indeed to affect their function seriously When contact is made with relatively low voltage electricity the *release of energy is insufficient to* cause severe local burning or generalized muscular spasm so that contact is maintained until the victim falls or is pulled away from the point of contact. Further if the hand is the point of contact local *muscle spasm in the forearm may* cause the hand to clench on the wire and so actually impede release In this way the heart and brain are subjected to a longer period of exposure to *the electric current* This causes cessation of respiration cardiac in hibition or fibrillation and loss of consciousness and unless respiration and circulation are promoted death must inevitably occur It cannot be too *strongly emphasized* that inability on the part of

CHAPTER 24

Poisons

CHARLES A ST HILL

THE diagnosis of poisoning may be a difficult matter and is one which is frequently missed Acute poisoning should be suspected when a person is affected with a group of symptoms of a definite character out of consonance with his previous state of health (Glaister) Suspicion will be strengthened if the symptoms arise shortly after a meal although of course certain natural diseases may arise with great suddenness and may be exacerbated by taking food Chronic poisoning usually shows itself insidiously and in some cases may mimic or be mimicked by natural disease It is in such chronic cases that the diagnosis may be missed unless the possibility of poisoning is borne in mind

If the practitioner suspects that a patient is being feloniously poisoned considerable medical and legal responsibilities fall on him. These should be lightened by calling in a colleague for consultation and removing the patient at once to hospital At the same time steps should be taken to confirm the suspicions by collecting specimens of faeces urine and vomitus for analysis These should be collected personally placed in chemically-clean containers and handed personally to the laboratory In view of the possibility of future legal action in which the doctor will be an important witness careful and full notes should be made at the time of all the features of the case These should include records of the exact times of onset or exacerbations of symptoms their relationship to food notes as to the presence or absence of similar symptoms in other members of the family and details of treatment. If the patient recovers in hospital but relapses on returning home and if the laboratory analysis confirms the suspicion of poisoning it will be necessary to take action to stop its continuation The method to be adopted depends upon the conditions but generally the patient should be told the facts and his permission obtained for informing the police If the patient dies and there is even a suspicion of poisoning the case should be reported to the Coroner immediately Until his representatives arrive steps should be taken to prevent any tampering with bottles medicines food vomitus etc which may be needed to help in the investigation of the case

General Methods of Treatment of Acute Poisoning In all cases the first step should be to remove the poison from the patient s stomach. The only efficient method of doing this is by passing a stomach tube and washing out the stomach and this should be the method employed in all cases of poisons taken by mouth unless they are of corrosive nature The patient should be laid down in the prone position with the head lowered so that in the subsequent washouts any water leaking around the tube will not flow into the respiratory passages The tube is passed down the oesophagus and if the patient is unconscious care should be taken that it has not been passed into the lungs This may be demonstrated by holding the end of the tube under water as the patient exhales when if the tube has been passed into the trachea bubbles will come out of the end Having ascertained that the tube has been correctly passed the stomach should be repeatedly washed out with approximately half pint volumes of tepid water the first two or three washings being kept for analysis The washings should be repeated until from 1 to 2 gal of water have been used *i e* 20 to 30 times After the last washout it may be possible to leave a specific antidote in the stomach if the poison is known If the poison is not known a general antidote may be used One of the best of these is a mixture of magnesium oxide 1 part tannic acid 1 part and activated medicinal charcoal 2 parts An emulsion of ½ oz of this in water will tend to adsorb any poison left in the stomach after lavage but the antidote should be removed later to prevent the adsorbed poison passing into the intestines where it may be removed from the antidote and absorbed into the body

If no stomach tube is available it may be necessary to attempt to evacuate the stomach by means of emetics or even by tickling the back of the throat in order to promote vomiting A number of emetics are available such as mustard or salt (a dessert spoonful in a cup of warm water) ipecacuanha

signs and symptoms dependent upon the take up of the radioactive substance in the body For example the take up of radioactive iodine by the thyroid may lead to myxoedema

The effect of single large exposures to radiation of the whole body depends upon the size of the dose If it is enormous as may happen in exposure to the radiations of an atomic bomb death may occur within minutes or hours and is preceded by vomiting diarrhoea erythema and oedema of the skin circulatory collapse and coma If the dose is smaller (about 500 roentgens) it will be followed in a few hours by prostration vomiting and diarrhoea Later the victim develops fever and in two or three days ulcers of the mouth and throat appear with localized or spreading infections elsewhere on the body Progressive pallor prostration and haemorrhages from the mucous membranes are evidence of rapidly advancing aplastic anaemia The patient may die rapidly from infection or linger for a few weeks before dying of intractable anaemia

If the body is exposed to lesser doses of radiation (less than 300 roentgens) the signs and danger are correspondingly reduced Patients under X ray treatment for malignant disease may show some of the milder symptoms especially if the treatment is directed at the abdomen or chest Complaint is made of general malaise anorexia and nausea and the temperature may be elevated More serious signs are changes in the blood picture suggesting the onset of marrow aplasia Minor changes such as a transient lymphocytosis or monocytosis are not uncommon but a falling platelet count progressive neutropenia or worst of all a falling red cell count should be looked upon with misgivings

Treatment. The most important part of treatment is the prevention of over exposure of personnel to radiation by the provision of proper working conditions screening of radioactive substances and machines and the education of workers as to the dangers of their occupation Periodic medical examinations and blood counts should be carried out If there is any evidence of reaction to exposure immediate removal of the individual with a re examination of these safety measures should occur If serious blood disease develops repeated blood transfusions and haematinics should be given in the hope that the marrow may recover

After-care. The main risks that follow corrosive poisoning are perforation of the stomach or oesophagus and oseophageal stricture The risk of perforation may be reduced by the avoidance of anything but fluids by mouth and if it should occur appropriate surgical measures must be taken

CORROSIVE POISONS WITH IMPORTANT SPECIFIC ACTIONS

Oxalic Acid and its Salts

The acid is used in a number of trades such as brass polishing straw hat making and bookbinding and domestically as a metal polisher and stain remover Both the acid and its salts are white crystalline substances and may be swallowed in mistake for such harmless remedies as Epsom salts

Ingestion of the acid or its salts in strong solution produces the usual picture of corrosive poisoning In addition it is very rapidly absorbed and produces both in strong and weak solution a profound central nervous system depression so that the early symptoms are quickly replaced by deepening coma rapid feeble irregular pulse cold clammy skin and slow gasping respirations As the coma deepens muscular spasms or convulsions may occur until death supervenes Death may take place very rapidly usually in less than 4 hr and occasionally in a matter of minutes

In addition to its corrosive action and central nervous system depression oxalic acid causes severe renal damage If the patient survives the acute attack therefore signs of renal tubular irritation or necrosis may be expected and will take the form of albuminuria haematuria and oliguria progressing in many cases to anuria Death may occur in this stage from renal failure Under favourable conditions diuresis supervenes which may be sufficiently marked to dehydrate the patient Urinary output usually slowly becomes normal after this with eventual recovery of the patient

Treatment. Because of the toxic action of oxalic acid after absorption even after neutralization the first step should be the removal of the poison from the stomach with subsequent thorough washouts of that organ This should be done by means of a stomach tube as unlike most of the other corrosives its central nervous system depression is more important than its corrosive action Calcium salts should if possible be used in the washouts since calcium oxalate is insoluble and therefore not absorbed into the system If coma supervenes this can be treated only on general lines If anuria develops fluid intake must be controlled so that sufficient fluid is given just to replace fluid loss and this should be combined with a high calorie low protein diet. Such treatment will avoid overhydrating the tissues and minimize the production of nitrogenous end products of protein metabolism Although the appearance of a diuresis is a favourable sign careful watch should be kept on the patient as the diuresis is uncontrolled and may be accompanied by excessive electrolyte loss Serial biochemical observations on the blood should be made and replacement therapy given as required

Phenol (Carbolic Acid) and the Cresols

Phenol and the cresols are widely used as mixtures in the home and form the basis of many common disinfectant fluids In industry the di and trichloro-compounds of phenol form the basis of many manufacturing processes These two substances have toxic effects very similar to those of phenol and are at least as toxic

The actions of all these substances are similar Strong solutions have a local corrosive action on the tissues In addition they are rapidly absorbed and having entered the body exert a profound depressant action on the central nervous system Unlike oxalic acid these substances are absorbed rapidly through the skin so that exposure of large areas of skin to their action may lead to the absorption of an amount sufficient to cause death from central nervous system depression Even weak solutions have occasionally caused serious effects after long application to large areas of burned or ulcerated skin

When taken by mouth these substances rapidly produce the symptoms of any other corrosive poison although with phenol pain may be less owing to its local anaesthetic action In a short time these symptoms become rapidly overshadowed by weakness giddiness and stupor advancing to coma and death As coma increases depression of the respiratory cardiac and other centres of the brain produces irregular stertorous breathing with cyanosis a rapid feeble pulse and subnormal temperature Since the pupils may also be contracted such cases may simulate opium poisoning The staining of the skin around the mouth where it has been corroded together with the characteristic smell of phenol should help to distinguish these two conditions however

If the patient survives the acute poisoning he is in danger of death from the damage that phenol

(1 5 to 2 g or 20 to 30 gr in water) or even tepid dishwater The most efficient is apomorphine (6 mg or about 1/10 gr by injection) but it must be remembered that this substance is itself a central nervous system depressant

Having evacuated and washed out the stomach the patient should be transferred to hospital where such measures as the administration of oxygen intravenous infusions and specific antidote therapy will be available

The Corrosive Poisons

This group includes the common strong mineral acids and alkalis together with such caustic substances as oxalic acid and its salts acetic acid phenol ammonia and a number of other less common chemicals The primary effect of all these compounds is intense irritation followed by destruction of the tissues with which they come in contact The symptoms and signs therefore are those that would be expected from large scale destruction of the alimentary tract In addition certain members of the group produce special symptoms due to some physical or chemical characteristic For example the more volatile substances such as ammonia hydrochloric acid and nitric acid may cause acute respiratory symptoms due to the inhalation of their fumes while oxalic acid and phenol exert a profound depression of the central nervous system after absorption In this section therefore the effects of destruction of the alimentary tract mucosa by these corrosives will be described first together with treatment This will be followed by a description of some of the more important members of the group that produce special symptoms and signs

General Effects Immediately upon taking the substance there is severe burning of the mouth throat and abdomen This is rapidly followed by violent retching and vomiting the vomitus containing altered blood in some cases The reaction of the vomitus will be strongly acid or alkaline depending upon the type of corrosive ingested

In association with the abdominal symptoms respiratory distress may occur This is particularly liable to happen after the ingestion of strong concentrations of the mineral acids acetic acid and ammonia Inhalation of the vapour of these substances may cause acute laryngeal oedema with hoarseness noisy dyspnoea or even asphyxia

Following the immediate symptoms progressive signs of shock appear with collapse thirst falling blood pressure rapid feeble pulse and oliguria In cases that are fatal in the acute stages death usually occurs about 12 to 24 hr from ingestion The most rapidly acting poisons in this group are oxalic acid and phenol which commonly cause death in 3 to 4 hr occasionally in less than an hour

Treatment of the General Symptoms The poisonous nature of these substances is due to their physically destructive action on the tissues Once their acidity or alkalinity has been neutralized they are harmless unless of course like oxalic acid or phenol they have a specific toxic action after absorption

The first step in treatment therefore consists in neutralization of the poison by a dilute acid or alkali and this should precede evacuation of the stomach In selecting the appropriate acid or alkali care should be taken that the one used should not give off gas when it comes into contact with the poison If this should occur acute dilatation of the stomach or even rupture of that organ may be caused For this reason carbonates or bicarbonates should be avoided and such alkalis as magnesium hydroxide or trisilicate and lime water used in the treatment of corrosive acids and dilute acetic acid vinegar or even lemon or orange juice for the alkalis

Having attempted to neutralize the poison the stomach should be evacuated In poisoning by the strong mineral acids and alkalis this should be done by means of emetics as the passage of a stomach tube in such cases may involve the risk of perforation of a partially eroded oesophageal wall In poisoning by oxalic acid its salts and phenol on the other hand risk of perforation is small while the toxicity of even the neutralized substances is high In such cases therefore a tube should be passed and the stomach evacuated and subsequently thoroughly washed out Finally in all cases some demulcent substance such as milk olive oil or white of egg may be given

While these procedures are being carried out measures to counteract shock and pain should be instituted and should follow the usual lines If the patient survives for a short time dehydration may become severe so that intravenous infusions of saline glucose or plasma may be needed

becomes more marked muscular cramps and con vulsions occur the patient becomes stuporose and finally passes into coma continuing to death which may occur in a few hours or be delayed for a day or two If a large dose of a soluble form of arsenic is taken the generalized symptoms may appear with little or no evidence of preceding gastro intestinal irritation

Subacute Poisoning This condition may follow the acute phase or may be produced by the ad ministration of repeated doses somewhat smaller than those necessary to cause acute poisoning Symptoms of gastro intestinal irritation are evident and their re appearance in patients who have just survived acute poisoning may lead to the unjustified assumption that a second dose has been adminis tered Nausea abdominal discomfort and lack of appetite occur and are accompanied by signs of generalized systemic poisoning These take the form of rapid wasting peripheral neuritis cardiac failure and suppression of urine while the particular affinity of arsenic for epithelial tissues may lead to the appearance of skin rashes herpes of the lips and conjunctivitis The symptoms progress leading to gross weakness and emaciation and may end in death in one or two weeks from the onset of the condition.

Chronic Poisoning In chronic arsenical poisoning due to repeated ingestion of small doses of arsenic or following temporary recovery from the effects of one or more large doses the full and widespread effects of the progressive inhibition of cell enzyme systems is seen Although all the systems of the body are affected epithelial tissues suffer most

The patient experiences loss of appetite with indigestion and nausea At the same time skin mani festations appear These take the form of eczema keratosis brittleness of the nails conjunctivitis and loss of hair Later a patchy brown discoloration of the skin may appear interspersed with areas of leucoderma Nervous symptoms are frequently prominent and include those of peripheral neuritis with paraesthesiae and muscle tenderness These progress to paralysis with consequent muscular atrophy which accentuates the marked cachexia already present Myocardial insufficiency aggravates the patient s condition and death occurs from cachexia and cardiac failure or may be accelerated by some intercurrent infection

Isolation of the Poison If arsenical poisoning is suspected samples of urine and faeces should be obtained for analysis Since arsenic is present in high concentration in epithelial tissues the finger nails and hair will also contain it and can be chemi cally analysed for its presence Hair in particular is a useful material for analysis since an estimate of the length of time that the poison has been absorbed can be made from the distance from the hair root in which arsenic can be found

Fatal Dose The form in which arsenic is given influences the size of the minimum dose necessary to cause death It is probable that 120 to 200 mg (2–3 gr) of a soluble compound is the minimum dose that has caused fatal acute poisoning In chronic poisoning very much larger amounts than this may accumulate in the body and it is difficult to assess the minimum amounts of arsenic that will prove fatal in divided doses over a period of time

Treatment *Acute Poisoning* Removal of the poison from the stomach by emetics or preferably gastric lavage is the urgent first necessity and should be instituted within an hour of the poison being taken if much hope of success is to be enter tained Freshly made ferric hydrate is an antidote if it can be prepared in time Following these initial steps treatment will follow the usual line for shock dehydration and collapse as they appear

Subacute and Chronic Poisoning The principle of treatment lies in the prevention of combination between arsenic and the sulphydryl groups of the enzymes The most successful drug for this purpose is 2 3-dimercaptopropanol better known as British Anti Lewisite (B A L) This substance bears two sul phydryl groups on a small molecule and therefore arsenic has a strong affinity for it and will combine with it in preference to the sulphydryl groups of the tissue enzymes Treatment should begin at the earliest possible moment In the first 24 hr intra muscular injections of 2 ml of B A L in oil should be given at 6-hourly intervals On the second third and fourth days this dose should be repeated at 12 hourly intervals followed by daily injections for another two or three days B A L injections are painful and the substance may produce symptoms of mild toxicity such as generalized muscle pain vomiting lacrimation and changes in the blood pressure If a second course has to be given for recurrence of symptoms of poisoning the dose should be halved and the possibility of the develop ment of hypersensitivity by the patient borne in mind

Lead

Whereas the main portal of entry of most of the metallic irritants is the mouth lead poisoning quite frequently occurs from absorption through the lungs or skin Because of this and its wide spread use in such processes as printing battery making paint manufacturing pottery and in many other industries it is the most important of all the metallic poisons Even with all the precautions used in industry about 100 cases of industrial lead

may cause to the renal tubules It is said that in these cases the urine may be green because of its content of the breakdown products of phenol but this is an unusual feature

Treatment As in oxalic acid poisoning the central nervous system depression outweighs in seriousness the local *corrosive action of these substances* For this reason prompt and complete evacuation of the stomach and treatment on the lines indicated under oxalic acid *poisoning should immediately* be instituted

MINIMUM DOSES OF THE CORROSIVE POISONS THAT HAVE KILLED ADULTS

Poison	*Dose*	*Usual time of death*
Sulphuric Acid	3 5 ml (1 drachm)	18–24 hr
Nitric Acid	7 ml (2 drachm)	18 24 hr
Hydrochloric Acid	14 ml (4 drachm)	4–30 hr
Caustic Alkalis	2 5 g (40 gr)	12–24 hr
Phenol	3 5 ml (1 drachm)	4 hr
Oxalic Acid	*2 g (30 gr)*	*10 min.–4 hr*

The Irritant Poisons

Poisoning associated with marked irritation of the gastro intestinal tract may be caused by a large number of substances These include mineral irritants such as the salts of many metals phosphorus dilute solutions of the corrosive poisons and irritants such as croton oil cantharides or large doses *of the milder vegetable irritants that are commonly* used for their purgative properties Poisoning due to the mineral irritants arises by accident particularly in industry or sometimes as a result of attempted homicide or suicide Poisoning by the vegetable irritants is most commonly seen as the result of their use in attempts to procure abortion since they form the basis of most of the pills sold for this purpose under a variety of names in certain shops

Although a very large number of metallic salts *if taken in large enough doses will cause symptoms* of gastro intestinal irritation with possible fatal results the most important members of this group are arsenic lead phosphorus and mercury The importance of these lies in the fact that small doses may produce serious results and that they also have marked toxic properties after absorption into the body

Arsenic

Arsenic is a favourite of the homicidal poisoner as it has little taste or smell is easily administered and when ingested is highly poisonous It occurs in many forms for example the oxide or sulphide and is present in a number of agricultural insecticides weed killers and in certain mouse and rat poisons *Homicidal poisoning* by arsenic is nearly always carried out by the addition of one of its salts to food but cases have been recorded of accidental poisoning due to prolonged vaginal application the use of creams and depilatory ointments on the skin and after the inhalation of the volatile arsenical compound arsine This last substance has a completely different action from the solid arsenicals producing fulminating haemolytic anaemia

It is probable that the toxicity of arsenic is due to its local irritation and to the affinity of its trivalent form for the sulphydryl (SH) compounds of the tissues This group is present in about 40 per cent of the enzyme systems upon which the cells depend for their metabolism The addition of arsenic to the group inactivates the enzyme systems with consequent damage to or destruction of the cells

Clinical Picture *Acute Poisoning* The rate of onset of symptoms of arsenical *poisoning is variable* A large dose of a soluble compound taken on an empty stomach may produce symptoms *in a few minutes Small doses of a relatively* insoluble compound taken with or after plenty of food may not produce any ill effects for several hours When symptoms appear they are due to a combination of the two separate actions of the substance a local irritant action on the gastro intestinal mucosa before absorption and a general *protoplasmic toxic action after absorption The relative* prominence of symptoms due to one or other of these actions is variable so that while some cases may show a predominance of gastro intestinal irritation others may show predominantly generalized symptoms

The gastro intestinal symptoms appear first and take the form of a burning pain *in the abdomen* accompanied by nausea followed by uncontrollable vomiting with diarrhoea The dehydration so produced leads to a lowering of the blood pressure a rapid feeble pulse and urinary suppression *These* symptoms are aggravated by the generalized action of the poison which itself causes profound circulatory collapse and respiratory *depression As the* effects of the absorbed poison on the body s tissues

by lowering the calcium and vitamin D intake and the substitution of ammonium chloride for the alkaline drugs This should be carried out most carefully so that the rate of mobilization of the lead does not become sufficient to cause the reappear ance of symptoms of poisoning

A recent development in the treatment of lead poisoning is the use of ethylenediamine tetra acetic acid (EDTA) which by its chelating action is able to combine with and inactivate lead in the red cells tissues and bones It is of great value in reducing both blood and depot lead in acute and chronic poisoning One gramme of the compound (com monly known by its proprietory name Versene) is added to half to one pint of normal saline and given by intravenous drip The dose should be given twice a day for five days and the course may be repeated once after two to three days rest

Phosphorus

Of the two forms of phosphorus red and yellow only the latter is poisonous In the past when match heads were made from yellow phosphorus both the acute form of poisoning and the chronic (phossy jaw) were not uncommon Since the cessa tion of the use of yellow phosphorus in this manu facturing process phossy jaw has become a rarity and cases of acute phosphorus poisoning occur mainly as the result of accidents or attempts at suicide or homicide The usual sources of the phos phorus in such cases are certain brands of rat and mouse poisons

Acute Poisoning Several hours may elapse be tween the ingestion of the poison and the appearance of symptoms These are due to acute gastro intestinal irritation and are similar to the acute stages of any acute irritant poison except that the eructations and vomit taste and smell of garlic and in the early stages the vomitus is said to be luminous in the dark The patient may die of shock dehydration and exhaustion in the first few hours but frequently the symptoms remit for a day or two At the end of this period the symp toms recur and their seriousness is augmented by the presence of acute liver necrosis with secondary renal failure The final stage of the condition there fore presents symptoms and signs which may be expected in acute liver failure from any cause such as acute hepatitis acute yellow atrophy etc Jaundice and purpura are prominent and are accompanied by abdominal distension often with oedema and ascites The urine becomes scanty and albuminous and the faeces are pale Death occurs in about a week and is preceded by uraemic coma

Isolation of the Poison. In the early stages phos phorus can usually be identified in the vomit and faeces If death is delayed for some days the identification of phosphorus in the organs may be difficult as it is converted to phosphates which are normal tissue constitutents

Fatal Dose The minimum fatal dose is probably about 120 mg (2 gr) but cases have recovered after ingesting larger amounts

Treatment Treatment consists in immediate thorough gastric lavage either with water or a 1 per cent permangate solution Fat containing sub stances should be avoided as they hasten absorp tion of phosphorus General measures for shock pain and dehydration should be instituted in the early stages and measures to reduce the effects of hepatic and renal failure employed later

Mercury

Metallic mercury is relatively harmless when taken by mouth as it is absorbed with difficulty unless in a very finely-divided state The mercuric salts being soluble are more toxic than the mer curous and are the cause of most cases of poisoning Since compounds of mercury are used fairly widely in such industries as explosive hat and thermo meter manufacture and are also constituents of a number of antiseptic fluids accidental and indus trial poisoning occasionally occurs Poisoning has also been known to occur after over-enthusiastic use of mercurial diuretics and even after prolonged application of mercury compounds to the skin or vagina because of the capacity of these body surfaces to absorb the substance

Acute Poisoning The early symptoms of acute mercurial poisoning are similar to those produced by any gastro intestinal irritant and usually appear within half an hour of ingestion If the patient sur vives for about three days however certain features make their appearance which may assist a diagnosis of mercurial poisoning These mainly affect the mouth and kidneys

The Mouth Examination reveals swelling and inflammation of the gums excessive salivation and a foul breath As the condition progresses the teeth may become loose and ulcers may develop in the oral (and nasal) mucosae

The Kidneys Tubular damage or necrosis is produced by mercury This causes albuminuria the presence of casts and a reduction of urinary volume which in severe cases may progress to anuria Uraemia results from this leading to coma and death in 5 to 10 days in the majority of cases

Chronic Poisoning This condition is seen occa sionally in workers using mercurial compounds (*e g* hatter s shakes) and takes the form of a slow de velopment of the oral and renal changes seen in the later stages of acute poisoning together with general

poisoning are notified annually this figure being about one tenth of the number 50 years ago Lead poisoning may also occur as a result of accident homicide or from the misuse of medical preparations of lead such as the administration of diachylon plaster for the purpose of procuring abortion

Clinical Picture The symptoms of lead poisoning may be acute or chronic

Acute poisoning This is usually due to the oral intake of lead acetate (sugar of lead) as this is the only common soluble lead salt

The symptoms are those of acute intestinal irritation The clinical picture is similar to that described for arsenic except that in the majority of cases constipation is present instead of diarrhoea and the stools when passed are dark coloured and offensive Death may occur in this phase or the condition may progress to the chronic form Sometimes renal damage may occur in the acute phase which may give place to a slowly progressive nephritis with eventual renal insufficiency hypertension uraemia and death

Chronic Poisoning This is by far the most common type of lead poisoning and is one which should be kept in mind when examining any lead worker who seeks medical attention Lead because of its slow excretion is a cumulative poison Within the body it is metabolized in the same way as calcium It is stored mainly in the bones but a certain amount may also be found in the liver Its storage in and liberation from the bones is influenced like calcium by parathyroid gland activity calcium and vitamin D intake and variations in the acid base equilibrium of the body These physiological facts may be helpful in the diagnosis of latent plumbism and for the treatment of manifest poisoning

The chronic toxic action of lead is exerted on all the tissues of the body producing progressive general debility and cachexia The more recognizable symptoms and signs are due to its effect on the central nervous system alimentary tract and bone marrow

Central Nervous System Symptoms The patient complains of severe frontal headaches irritability and drowsiness At the same time nervous paralyses may occur the groups of muscles supplied by the affected nerves undergoing atrophy The commonest to be affected are the extensor muscles of the forearm with the production of wrist drop but other groups may be affected later In more severe or more acute cases optic atrophy mental confusion muscular inco ordination or even convulsions may occur (lead encephalopathy)

Blood Changes The earliest change in the blood picture is the appearance of red cells showing basophilic stippling Such cells may occur in small numbers in any severe anaemia and in most lead workers even though they have not absorbed excessive quantities of lead Their occurrence in relatively large numbers in the presence of only a mild anaemia or even no anaemia is strong evidence of lead poisoning In the routine blood examination of lead workers a proportion of more than three stippled cells per thousand red cells is taken as evidence of excessive lead absorption In more severe cases of lead poisoning a moderate degree of anaemia develops This is mainly haemolytic in origin and in consequence a tinge of jaundice may be noticeable on clinical examination of the patient

Alimentary Tract Symptoms These take the form of intermittent bouts of colic and constipation Examination of the mouth may reveal a blue line in the gums around the bases of carious teeth

Isolation of the Poison During life samples of urine and faeces may be examined The normal lead content of urine is less than 0 02 mg/l and the normal faecal output is less than 0 3 mg/day In lead poisoning these figures may be greatly exceeded

Fatal Dose 2 to 3 g (30 to 45 gr) of lead acetate is probably the minimum that may cause death but recovery has occurred after the ingestion of much larger amounts The absorption of 1 to 2 mg daily is sufficient to produce cumulative effects with evidence of chronic poisoning in time

Treatment *Acute Poisoning* Gastric lavage should be instituted using solutions of magnesium or sodium sulphate in a strength of 2 oz/gal These form an insoluble precipitate with lead which should be removed by copious washouts with water At the end of the lavage some magnesium sulphate may be left in the stomach as this will not only neutralize lead that may be present in the intestines but will also combat constipation

General treatment of shock and dehydration should be instituted if necessary Calcium gluconate may also be given intravenously

Chronic Poisoning In industry a considerable reduction in the incidence of chronic lead poisoning has been achieved by the provision of good working conditions The basis of treatment of chronic poisoning is to remove the lead from the blood stream either through the normal excretory channels of the kidneys and bowel or by stimulating absorption into the bones Since an effectively increased excretion of lead through the normal channels can not be achieved the first stage in treatment is to promote its deposition in the bones by the administration of alkalis a high calcium diet and vitamin D When symptoms have been relieved a gradual removal of lead from the bones may be obtained

Aspirin

Because of the widespread use and free availability of this drug and its related compounds it is commonly used as a suicidal agent Apart from its depressant action on the central nervous system when taken in large doses it has a number of side actions which affect the symptomatology of acute poisoning It has an irritant action on the gastric mucosa which before coma occurs may give rise to epigastric discomfort eructations or even vomiting the last sometimes thwarting the intention of suicide Gastric irritation may be of sufficient intensity to produce bleeding with consequent haematemesis indeed this may occasionally occur after repeated therapeutic doses In the early stages of poisoning hyperpnoea may result from the increase in metabolic rate produced by aspirin as well as from its acidotic effect The coma of aspirin poisoning therefore may simulate that of diabetes or uraemia Confusion between diabetic coma and that of aspirin poisoning may be accentuated by the fact that the excretion of large amounts of salicylates in urine may produce not only a positive ferric chloride test but occasionally causes reduction of Benedict s reagent.

Fatal Dose. There is considerable variation in susceptibility to the effects of aspirin Deaths have been reported after as little as 6 5 g (100 gr) but many patients have survived doses two or three times as large In certain individuals idiosyncrasy to the drug may produce sudden severe symptoms such as giant urticaria abdominal pain and vomiting after small therapeutic doses

Treatment The drug should immediately be removed from the stomach by intubation and repeated washouts Depression of the respiratory and cardiac centres may be influenced by injections of nikethamide or picrotoxin but the convulsive properties of the latter must be borne in mind if repeated doses are given Oxygen may be administered if necessary by endotracheal tube to stimulate respiration If acidosis is present it may be counteracted by the intravenous infusion of isotonic sodium bicarbonate but the amount given must be controlled by serial plasma alkali reserve estimations Sodium bicarbonate administration also increases the rate of removal of salicylates by the kidneys

Barbiturates

These substances are second only in importance to aspirin as agents for suicide and in addition have been responsible for many deaths from accidental over-dosage Some of these cases have been due to the fact that the effects of barbiturate are considerably potentiated by alcohol so that the ingestion of a dose of barbiturates which alone would produce little ill effect may cause death if the recipient then drinks large quantities of an alcoholic beverage Other cases may have been due to the reputed amnesic effect of the drug which is said to result in a lack of realization that a dose has been taken so that it may be repeated one or more times until a fatally large quantity is ingested

The rapidity of onset of coma in cases of over dosage by the barbiturates together with the length of time elapsing before death supervenes in fatal cases depends upon the dose and the type of barbiturate taken The long acting barbiturates such as phenobarbitone or barbitone itself may have little effect for an hour or two after administration and may persist in the body and continue to produce cerebral depression for 24 hr or more At the other end of the scale short acting barbiturates such as pentobarbitone and cyclobarbitone or the very short acting derivatives such as thiopentone sodium may act with great rapidity but their action persists only for a short time

Fatal Dose This depends upon the type of barbiturate taken particularly upon its rate of absorption Thus the longer acting drugs will probably not prove fatal unless doses in the order of 3 2 g (50 gr) or more are ingested whereas the very short acting types may produce death in doses as low as 1 g (15 gr)

Treatment. The initial step should be the removal of the poison from the stomach by repeated gastric lavage Depression of the cardiac or respiratory centres may be combated by the administration of oxygen in combination with intravenous injections of nikethamide (1–4 ml) picrotoxin (2–5 ml) amphetamine (2 5–10 mg) or leptazol (100–200 mg)

It may be necessary to repeat these doses at 15 min intervals until the patient begins to show signs of diminishing coma At this stage intravenous injections should be replaced by intramuscular and the doses of stimulating drugs reduced Throughout treatment, careful watch should be maintained for evidence of over-dosage by these central nervous system stimulants which may show itself as muscular twitchings or frank convulsions Recently drugs such as bemegride (Megimide) and amiphenazole (Daptazole) have been used with considerable success for the relief of barbiturate coma It is claimed that not only do these drugs stimulate the respiratory and other vital centres but that other evidences of deep coma such as loss of pupillary reaction to light and loss of muscle tone and laryngeal reflexes are counteracted Relatively large volumes of fluids containing these drugs must be injected so that it is probably best to set up an

muscular wasting and central nervous system changes In addition to the salivation gingivitis and loosening of the teeth a blue black line may some times be seen on the gums around the bases of the teeth The renal damage is slowly progressive and clinically resembles chronic nephritis leading finally to uraemia Involvement of the central nervous system manifests itself as intention tremors of the muscles of the tongue face arms and later the legs Mental disturbances may occur causing irritability loss of memory hallucinations or even mania The condition progresses slowly and is accompanied by wasting

Fatal Dose 200–300 mg (3 to 5 gr) of the soluble mercury salts taken by mouth are sometimes suffi cient to cause death although recovery may occur after larger doses Mercury preparations containing about twice this dose have been known to cause death after absorption from the vagina

Treatment Repeated gastric lavage forms the basis of treatment of acute poisoning The effective ness of this may be increased by the preliminary administration of an albuminous fluid such as egg white which forms a complex with mercury This complex is insoluble in water but is soluble in excess of albumin so that it must be removed by lavage as soon as possible In order to combat the effect of absorbed mercury *B A L* may be adminis tered in the same manner as for lead poisoning though because of the rapid absorption of mer cury and the consequent high concentration that *may occur in the blood stream somewhat larger* doses may be needed In such cases the patient should be observed for any evidence of the toxic effects of B A L itself If the patient survives the earlier stages of poisoning treatment should be directed at counteracting as far as possible the effects of the renal failure caused by lower nephron destruction In the oliguric phase this will necessi tate the control of water and protein intake to gether with the administration of large amounts of carbohydrate In the later polyuric phase if the patient reaches it the measurement and replacement of water and electrolyte loss will be needed

Poisoning by other Metals

Cases of poisoning by salts of antimony copper iron zinc tin and barium occasionally occur Of these metals antimony in the form of tartar emetic is the best known poison The symptoms of poisoning by all these metals are similar being those of acute intestinal irritation with dehydration and collapse if the amount taken is sufficient It should be remembered that the common medicinal form of iron—tab ferri sulph —may act as an irritant poison if taken in sufficient quantity A few cases of death in infants who had taken a number of these tablets have been reported

Non metallic Irritants

Substances of this class such as castor oil croton *oil cantharides aloes jalap scammony etc may* be taken by accident or with the intention of produc ing abortion since they are common ingredients of the remedies for female ills that are sold in cer *tain shops Their abortifacient properties* are probably entirely dependent upon the intestinal irritation and pelvic congestion they produce If large doses are taken violent purging with dehydra tion collapse and even death may occur

The Cerebral Depressants

This group of substances includes the hypnotic and narcotic drugs These may be divided into several classes—

(*a*) Simple analgesics such as aspirin phenacetin acetanilide and amidopyrin
(*b*) Hypnotics such as the barbiturates the sul phone derivatives paraldehyde and chloral
(*c*) Opium alkaloids such as morphia and its relatives and synthetic substitutes such as pethidine and amidone
(*d*) Anaesthetic drugs such as ether chloroform trichlorethylene (trilene) and most important of all alcohol

Death from overdosage of any of these drugs is due to progressive central nervous system depres sion leading finally to respiratory failure so that the basic signs and symptoms are similar for them *all Ingestion of the drug is followed* by drowsiness stupor and later unconsciousness which deepens steadily As the respiratory centre becomes depressed respiration becomes shallow slow or of *Cheyne Stokes type* This is accompanied by cya nosis and variable evidence of depression of the cardiac centres in the terminal stages In addition to the symptoms common to patients affected by overdoses of these drugs certain special symptoms or signs may be present in poisoning by some indi vidual members of the group These drugs are dis cussed separately below

proper control of the vehicle (Road Traffic Act 1930)

For these reasons it is important that the medical practitioner should be able not only to recognize frank drunkenness and alcoholic coma but to differentiate these conditions from others that may mimic them and to be able to assess minor degrees of inebriation and its mimics

The effect of alcohol is a progressive depression first of the cortical areas controlling behaviour then of the centres controlling voluntary movement and logical thought followed by stupor and coma

The first effect is a slackening of the reserve normally imposed by habit and custom with a slight dulling of mental sensitivity At this stage the drinker s troubles seem less he feels more cheerful perhaps vivacious and talkative Life seems generally brighter jokes appear to be funnier and his own conversation much wittier This is accompanied by imperceptible dulling of the finer degrees of physical control and a definite increase of the reaction time This stage which is commonly seen after the first round of drinks at a cocktail party is often succeeded by a feeling of superb confidence It is this stage that is very dangerous to drivers for they feel that they are driving very skilfully and this encourages them to take risks they would otherwise avoid while at the same time their reaction time is greater and their driving capability less than normal

A stage further sees motor function affected The slurred speech and lurching gait of the man one over the eight" is so familiar as to be a music hall joke and needs no further description The mental state at this stage may be one of glorious detachment when all the world is surveyed and set to rights by mere eloquence or may be one of simple belligerence fighting drunk Logical thinking and reasoning are all but impossible at this stage but it is important to realize that to the individual concerned the conversation is perfectly logical On his recovery he may not believe that he has been talking nonsense From motor instability and muddled thought the descent to stupor and coma is simply progressive

The diagnosis of drunkenness in its severe forms may well be obvious but the possible presence of other conditions which may simulate it or aggravate the effects of a moderate intake of alcohol must be borne in mind Perhaps the most important of these is an injury to the head which may have been inflicted on an already inebriated person who has subsequently lapsed into coma The fact that such a patient smells of drink and may be known to have been severely intoxicated before the injury was received should not deter the medical examiner from weighing very carefully the possibility as to whether a serious intracranial haemorrhage may be present Other conditions which may mimic or aggravate the effects of alcohol are diabetic coma uraemia hypoglycaemia vascular catastrophes such as cerebral thrombosis neurological disorders such as epilepsy disseminated sclerosis and intracranial tumours and the effects of such drugs as barbiturates the antihistamines atropine hyoscine and a number of others Finally the effects of exposure to carbon monoxide from faulty car-exhaust systems may occasionally give rise to symptoms resembling drunkenness These conditions must be excluded before a diagnosis of drunkenness is made particularly if the patient under investigation has been involved in a motor car accident and is therefore liable to be charged with being under the influence of drink to such an extent as to be incapable of having proper control of a car A full clinical examination should always be carried out and notes made at the time These notes should include details of the patient s state of dress his recollections of his movements for some hours before the examination and his general manner and behaviour His memory manner of answering questions and clarity of diction (or lack of it) all help to build up a picture of his state After the physical examination has been completed tests may be made to assess his mental acuteness and muscular co ordination These tests should be simple and the unfortunate examinee should not be asked to walk along straight lines or repeat tongue twisters He may be asked to write his name and address copy a piece of printing or carry out simple addition or subtraction sums but in assessing even these results due consideration should be given to nervous stress and his probable standard of education In order to assist the clinical examination samples of urine or possibly blood may be taken so that their alcohol content may be estimated Of the two it is more advisable to take urine so as to avoid the necessity of venepuncture and a sample should be taken at the beginning and at the end of the interview No hard and fast interpretation can be made of the concentrations of alcohol found in blood and urine for the obvious reason that individual reaction to a particular alcohol concentration is variable The minimum intake of alcohol necessary to produce various blood or urine levels can be calculated from a knowledge of the alcohol content of various beverages and the weight of the individual Thus a urinary alcohol level of about 100 mg per 100 ml is equivalent to a minimum intake of about 2 pints of ordinary beer in an eleven stone man

Methyl Alcohol (Wood Alcohol) This has intoxicating effects similar to but more serious than those of ethyl alcohol It is used commercially in large

intravenous drip of glucose or saline and inject the drugs into the rubber tubing of the drip close to its attachment to the intravenous needle 15 mg of amiphenazole in 1 ml of water and 50 of bemegride in 10 ml of water are injected at 3 to 5 minute intervals until the patient reaches a state of light anaesthesia At this stage which should be reached within 2 hr the treatment should be stopped and the patient allowed to recover spontaneously These drugs may cause convulsions so that the appearance of muscular twitchings should be a warning to reduce the dosage

If convulsions occur small doses of intravenous thiopentol may have to be given

If the coma lasts for many hours the presence of hypostatic congestion of the lungs with a considerable risk of bronchopneumonia should be borne in mind and antibiotic therapy may have to be instituted to prevent this complication

Other drugs in this group rarely produce fatal poisoning due to cerebral depression although some of them may produce important toxic side effects Amongst the most important of these are amidopyrin which may produce a serious neutropenia and sedormid which in a small proportion of cases produces purpura

Opium Alkaloids and Their Substitutes

Because of the stringent regulations controlling the sale of these drugs acute poisoning by any of them is uncommon The expected symptoms of advancing central nervous system depression are present with additional signs which should aid diagnosis These are first the presence of contracted pupils which may be so small as to warrant the name pin point and secondly a tendency for the patient's temperature to fall This is accompanied by profuse sweating so that the skin feels cold and clammy to the touch Respiratory depression is marked and may terminally be Cheyne Stokes in type

Although these drugs do not commonly cause acute poisoning their capacity to cause habit formation is powerful and important The worst of all these drugs in this capacity is probably heroin and for this reason its manufacture and use has been banned in many countries The morphia substitutes such as pethidine which it was hoped would prove to have little habit forming properties are quite as dangerous as morphia in this respect and pethidine itself is now probably responsible for more addiction than any of the members of this group

Fatal Dose The minimum fatal dose for an adult is probably about 120–300 mg (2–3 gr) of morphia provided no tolerance has been acquired by repeated administration Confirmed addicts regularly take daily doses far in excess of this On the other hand infants and young children are exceedingly susceptible to these drugs and may succumb to doses well below 15 mg (¼ gr)

Treatment In acute poisoning due to oral intake the stomach should be washed out immediately If poisoning is due to the injection of one of these drugs lavage is obviously useless and treatment should aim at counteracting depression of the vital centres particularly the respiratory centre Oxygen together with the various central nervous system stimulants may be used Particularly recommended in this connexion is amiphenazole (Daptazole) which can be given by intravenous or intramuscular injection in 20 mg doses These may be repeated at 10 min intervals until 200 mg have been given by which time respirations should have become deeper and more efficient This drug is claimed to have a very marked effect in maintaining not only respiration but also consciousness in the presence of very large doses of morphia and its allied compounds

Anaesthetic Drugs and Alcohols

Overdosage or death occurring during the administration of ether chloroform trichlorethylene etc is of course one of the possibilities that must lie at the back of the mind of the anaesthetist A discussion of anaesthetic risks is beyond the scope of this section and for information on this matter reference should be made to specialized books on the subject

Ethyl alcohol is chemically related to these accepted anaesthetic substances and of all the drugs that are taken in excessive quantities it is the most important Although deaths from acute alcohol poisoning are uncommon victims of lesser degrees of over-dosage are frequently seen by the medical practitioner

Individuals who have been drinking may be brought to the doctor because they are severely drunk and in danger of passing into coma or because they require examination as a result of some accident that may have befallen them after having taken an unknown quantity of alcohol For instance a man may be admitted unconscious to a Casualty Department after a drunken brawl and it may be exceedingly difficult but very important to determine whether his unconsciousness is due to injury or a grossly excessive alcoholic intake Alternatively he may have been involved in a motor accident and be presented to the doctor as someone who when driving or attempting to drive or when in charge of a motor vehicle on a road or other public place is under the influence of drink or a drug to such an extent as to be incapable of having

convulsions dilated pupils and sometimes death from cardiac and respiratory failure Occasionally particularly in patients who are sensitive to the drug death may occur with startling rapidity

Treatment Any remaining drug should be removed if possible If it has been taken by mouth gastric lavage should be performed if applied locally the surface should be thoroughly washed After this measures similar to those recommended for atropine poisoning should be instituted with the exception of course that prostigmine and its related drugs are of no value

Chronic Poisoning Cocaine is a powerful drug of addiction because of the mental stimulation that it produces Treatment of this condition is carried out on the same lines as that of morphia addiction

Strychnine

This potent poison is occasionally used for suicidal or homicidal purposes but owing to the regulations governing its sale cases are rare Accidental poisoning may also occur although the extremely bitter taste of the substance makes it unpalatable The drug greatly increases the sensitivity of the central nervous system reflexes If therefore it is taken in excess the slightest stimulus produces a shower of motor impulses throughout the body that result in a sudden violent spasm of all muscles The victim becomes rigid with the back arched and the facial muscles fixed in a rigid grin (risus sardonicus) The respiratory muscles are involved in the spasm resulting in deep cyanosis As the convulsions continue and become prolonged increasing asphyxia occurs until finally it produces death Consciousness is retained until the end

Fatal Dose About 30 mg (½ gr) has caused death Death usually occurs in a few minutes to an hour

Treatment. The immediate necessity is to overcome the convulsions as it is these that produce death from asphyxia This can be done by anaesthetizing the patient and only when this has been effected is it possible to perform gastric lavage As the effects of the poison wear off full anaesthesia may be replaced by sedation by barbiturates chloral or bromides

Other Nervous-system Poisons

Poisoning by other drugs primarily affecting the nervous system may occasionally be seen The most important of these are probably camphor which is easily obtained in the form of moth balls and liniments nicotine and certain organic alkyl phosphates which are widely used as insecticides These substances produce rapid collapse vomiting convulsions and finally death from cardiac and respiratory failure

The Asphyxiants

This group of poisons includes those substances which in one way or another prevent oxygenation of the tissues The poison gases of war such as chlorine and phosgene which cause asphyxia by producing acute irritation and oedema of the respiratory system together with all those gases which may displace oxygen from the atmosphere are members of this group but are of little importance Carbon monoxide by its power of displacing oxygen from haemoglobin and hydrogen cyanide because it prevents the tissues utilizing oxygen also fall into this group and are the only members that need description

Carbon Monoxide

Poisoning by carbon monoxide is extremely common since this gas is a constituent of ordinary household coal gas and is produced by most combustion processes Household coal gas contains about 10 per cent carbon monoxide while car exhaust fumes contain only slightly less Any heating stove or fire produces a proportion of carbon monoxide particularly if combustion is not complete Since incomplete combustion may well be produced by lack of ventilation the concentration of carbon monoxide in the vicinity of a fire or stove under these conditions may steadily rise Carboxyhaemoglobin is about 200 times as stable as oxyhaemoglobin so that the presence of relatively small quantities of carbon monoxide in the atmosphere will lead to an accumulation of carboxyhaemoglobin in the blood stream No noticeable symptoms are produced by concentrations of less than 20 per cent carboxyhaemoglobin but when this level is attained headache and dizziness may be experienced If the concentration rises to 40 per cent mental confusion drowsiness ataxia and muscular weakness occur which become more severe until by the time the blood contains 50 to 60 per cent unconsciousness occurs and if the subject is not rapidly removed from the atmosphere death supervenes The rate of onset of these symptoms varies of course with the concentration of carbon

quantities but is not easily obtained by the ordinary citizen except in methylated spirits which consist of about 90 per cent ethyl and 10 per cent methyl alcohol The dangers of methyl alcohol drinking lie in the fact that unlike ethyl alcohol oxidation in the body is slow and the products of oxidation formic acid and formaldehyde are highly toxic

Symptoms These may be delayed for some hours after drinking the fluid and then appear with great suddenness They take the form of headache vomiting and muscular weakness leading to coma which may be preceded by violent maniacal behaviour The toxic effects may last a long time because of the inability of the body to metabolize and excrete methyl alcohol and several days may elapse before all of it is removed from the body Because of this the treatment of methyl alcohol poisoning should be prolonged and the patient kept under observation after the acute symptoms have passed In all cases of methyl alcohol poisoning whether they are due to one large dose or several small ones blindness due to optic atrophy is liable to occur

Treatment. The treatment of ethyl alcohol poisoning will depend upon the degree of intoxication If this is relatively mild it may only be necessary to ensure that the patient does not harm himself or others e g by driving a car and that he should be put to bed to sleep it off If the degree of intoxication is severe the remains of his imbibed drink should be removed As in any form of poisoning the best means of doing this is by the use of a stomach tube but emetics may have to be used if a tube is not available After removing the alcohol and washing out the stomach stimulants ranging in potency from coffee to nikethamide may have to be prescribed If respiratory depression is present oxygen may be necessary

In methyl alcohol poisoning respiratory depression may be marked and should be watched for In addition the acidosis produced by the acid end products of methyl alcohol katabolism should be treated by the administration of sodium bicarbonate by mouth or intravenously as the case may warrant

Nervous System Excitants and Irritants

There are many substances having a direct action on the nervous system which if taken in excessive doses may act as rapidly fatal poisons Although poisoning by such substances is uncommon a few of the more important members of this group need description

Atropine and its Related Alkaloids Hyoscyamine and Hyoscine

Poisoning by these substances may follow accidental or intentional ingestion of the purified alkaloids or by eating seeds and fruits containing them in their crude form e g deadly night shade (belladonna) In pharmacological doses the pure drugs act as parasympathetic inhibitors but in larger doses atropine and hyoscyamine produce marked cerebral and medullary stimulation so that cases of poisoning show features due to both these actions Hyoscine does not have a similar stimulating affect on the central nervous system overdosage resulting in cerebral depression without any primary excitory phase

Clinical Picture In the early stages there is restlessness mental excitement and talkativeness progressing to wild purposeless movements of the limbs hallucinations delirium or even violent mania At the same time the mouth and respiratory passages become exceedingly dry causing the voice to be husky and swallowing difficult The skin is flushed the pulse is increased and the pupils are widely dilated and unresponsive to light If the dose taken is large enough this stage of excitement gives way to one of progressive central nervous system depression The patient passes into coma pulse and respirations become progressively slower until death supervenes usually in 24 to 48 hr

Fatal Dose About 120 mg (2 gr) of atropine and 30 mg ($\frac{1}{2}$ gr) of hyoscine have caused death Children who have eaten quite small numbers of belladonna berries may show severe poisoning and death has occurred after eating less than twenty

Treatment The stomach should be evacuated by lavage as soon as possible Many of the effects of the atropine group of drugs can be counteracted by prostigmine pilocarpine or physostigmine If cerebral excitement is severe short acting barbiturates may have to be administered or even a general anaesthetic In the stage of depression stimulants oxygen and carbon dioxide and artificial respiration may be necessary

Cocaine

This substance may cause acute poisoning either because of overdosage or because of individual hypersensitivity to medicinal doses The symptoms and signs are not unlike those of atropine the patient undergoing a short stage of physical and mental excitement followed by sudden collapse

difficulty of speech and paraesthesiae of the limbs This is followed by advancing cerebral depression coma and death in about 10 per cent of cases

Chronic benzene poisoning mainly affects the haemopoietic system The bone marrow undergoes patchy asplasia interspersed with areas of hyperplasia In the early phases this may result in leucocytosis or polycythaemia in the peripheral blood In a proportion of cases the leucocytosis may be very marked and eventually progresses to true leukaemia with death from this condition More commonly the aplasia of the marrow outstrips the hyperplasia resulting in thrombocytopenia agranulocytosis or aplastic anaemia with all the symptoms and signs associated with these blood changes In some cases haemolytic anaemia is also present with mild jaundice and reticulocytosis

Treatment. The prognosis is poor in those cases in which evidence of serious marrow aplasia is present Liver preparations nucleic acid derivatives and vitamin C have all been used and have occasionally been followed by transient improvement The most useful treatment is repeated blood transfusion in the hope that if the anaemia can be combated for a sufficient time whilst the patient is kept away from the source of poisoning his bone marrow may recover

Fatal Dose There is a very great individual variation in sensitiveness to the toxic action of benzene some individuals being very susceptible and others being apparently unaffected by large and continued dosage

The Nitrobenzenes Aniline and Nitroanilines

These compounds have an effect on the central nervous system similar to benzene but varying in intensity Their best known effect is on the haemoglobin which is converted to methaemoglobin This imparts a brownish colour to the blood which causes the patient to appear cyanosed. More important it reduces the oxygen carrying capacity of the blood so that a general tissue anoxaemia results The victim complains of disturbance of vision tinnitus headache and nausea Later twitchings paraesthesiae and paralysis of the legs occur followed by convulsions coma and death from cardiac or respiratory failure

Minor absorptions of these compounds over a period of time may lead to a milder degree of methaemoglobinaemia in which the patient complains merely of lack of energy and dyspnoea on exertion Examination in a good light may reveal cyanosis and blood examination will reveal anaemia and the presence of a moderate amount of methaemoglobin

Treatment. Remove the patient from the source of poisoning and if it has been swallowed wash out the stomach The most important principle of treatment is to combat the decreased oxygen-carrying capacity of the blood Some good may be derived from the administration of oxygen or exchange transfusions may be attempted in serious cases A single oral dose of tetramethylthionine chloride (purified methylene blue) 120 mg may be sufficient to eliminate the cyanosis Repeated doses of ascorbic acid have a similar effect

Fatal Dose This is difficult to estimate but cases have been reported in which death has followed the ingestion of 1 ml of some of these compounds

Trinitrotoluene

This substance is used extensively in explosive manufacture so that cases are particularly liable to be seen in wartime It is absorbed through the skin alimentary tract, or lungs and may cause local irritation in any of these situations Personnel handling this material may suffer from eczematous rashes with yellow staining of the skin chronic cough nasal discomfort gastric pains anorexia and vomiting Its more serious effects are concentrated on the haemopoietic tissues and liver The effects on the blood result in a haemolytic anaemia which may later become aplastic in type The liver may undergo massive necrosis with all the signs and symptoms of acute liver failure

The Chlorinated Hydrocarbons

These compounds such as carbon tetrachloride trichlorethylene tetrachlorethane and many others are becoming widely used in industry The danger to industrial workers depends upon the compound being used since their toxicity varies The symptoms produced are caused either by central nervous system irritation or depression or by liver and renal failure due to necrosis of these organs

monoxide in the atmosphere If it is about 0 1 per cent some hours may elapse before the person becomes unconscious whereas if it is 2 per cent death may occur in a few minutes Since exercise increases the respiratory rate it also causes a more rapid uptake of carbon monoxide so that a person at rest who realizes that there is carbon monoxide in the atmosphere and attempts to get out of danger quickly may so increase respiratory exchange that unconsciousness rapidly supervenes High metabolic rate and respiratory exchange is also the explanation of the high susceptibility of children small animals and particularly birds to carbon monoxide poisoning and it is for this reason that canaries have been used by miners for the detection of fire damp for many years

Diagnosis This is made by a history of exposure to fumes or products of combustion and the condition of the patient If the concentration of carboxyhaemoglobin rises to about 35 per cent the blood and probably the patient s skin may be noticeably pink in colour although the skin coloration is more easily seen after death when the appearance of hypostatic lividity makes it obvious In the absence of a history of exposure to carbon monoxide diagnosis may be difficult and some cerebral catastrophe coma due to diabetes uraemia drugs or most important of all drunkenness may be suspected

Treatment Immediate removal of the victim from the poisonous atmosphere is the obvious first step Subsequently treatment will depend upon the severity of poisoning If the patient is unconscious and respirations are shallow artificial respiration with application of 5 per cent carbon dioxide in oxygen may be necessary In extreme cases an exchange transfusion of several pints of blood may prove of benefit In all cases it should be remembered that the chief danger to the patient is cerebral and cardiac anoxaemia The brain can only exist for a short time with insufficient oxygen and even if recovery occurs central nervous system changes may be evident either temporarily or permanently

Hydrocyanic Acid (Prussic Acid)

Hydrocyanic acid is fairly commonly used as a fumigant for fruit tree pests and for the destruction of vermin such as wasps rats and mice Its common sodium salt is also used in photography but since it is rapidly converted to hydrocyanic acid by the hydrochloric acid of the stomach it is equally as lethal as the acid Hydrocyanic acid itself can be recognized by its smell of bitter almonds and since its salts are slowly converted to the acid by the atmosphere they too give off a similar but faint smell This smell is not recognizable by everybody only about one person in every three being able to detect it unless it is present in high concentration

Clinical Picture The action of hydrocyanic acid is immediate but there is a few minutes delay after taking the salts When symptoms appear they advance to death with extreme rapidity the patient becoming dizzy losing muscular power and collapsing within a few seconds Because of the inability of the tissues to utilize oxygen both the venous and arterial blood remains bright red After death therefore the skin particularly in the hypostatic areas is pink in colour and the appearances may resemble those of carbon monoxide poisoning

Treatment Death occurs so rapidly that it is very unlikely that there will be time for treatment to be carried out once the symptoms have appeared If it is known that potassium cyanide has been swallowed and symptoms have not yet begun there may be time to perform gastric lavage and to introduce a solution of sodium thiosulphate down the tube into the stomach

Fatal Dose About one part in two thousand of hydrogen cyanide in the atmosphere will produce fatal symptoms Probably about 300 mg (5 gr) of sodium of potassium cyanide will produce a fatal result when taken by mouth

Benzene and its Derivatives

Benzene and the chemicals derived from it such as toluene aniline and phenol together with their nitro amino and other derivatives are widely used in industry as solvents Many of these very numerous substances have serious toxic properties and since some of them are readily absorbed through the skin their dangers are enhanced The number of these industrial solvents is large and each one produces its own symptomatology Only a few of the more important compounds can be described here

Benzene

Poisoning by this substance is usually chronic due to inhalation of the vapour but may occasionally be acute If large doses are absorbed they cause acute central nervous system depression In the early stages there is headache nausea mental confusion

Chlorides (as NaCl)	10–15 g per diem
Diastase	8 000–30 000 Wohlegemuth units per diem.
	6–33 Wohlegemuth units per ml
Potassium	2–4 g per diem.
Sodium	3–6 g per diem.
Urea	16–35 g per diem
17 Ketosteroids	Up to 7 years 0 5–2 5 mg per diem.
	8–12 years 2–5 mg per diem.
	12–15 years 5–11 mg per diem.
	Adult men 9–24 mg per diem.
	Adult women 5–17 mg per diem.

Faeces

Amount	Adult on mixed diet 60–250 g moist faeces per diem
Fat	Adults 10–25 g per 100 g dried faeces
	Infants up to 35 g per 100 g dried faeces
Fat balance	In adults not more than 10 per cent of a fat intake of 70 g per diem should be excreted
Urobilinogen	30–220 mg per 100 g

Cerebrospinal Fluid

Cells	0–3 lymphocytes per c mm.
Protein	15–40 mg/100 ml
Glucose	50–90 mg/100 ml.
Chlorides (as NaCl)	700–740 mg/100 ml

Haematological Normals

Blood volume	4–8 litres (78–97 ml/kg of body weight)
Haemoglobin	Adult males 14–17 g/100 ml
	Women and children, 12–15 2 g/100 ml.
Erythrocytes	Adult males 4 5–6 4 million per c mm.
	Women and children, 4·0–5 5 million per c mm.
Leucocytes	4 000–11 000 per c mm
Neutrophil polymorphonuclears	2 000–7 500 per c.mm.
Lymphocytes	1 000–3 500 per c mm
Monocytes	0–800 per c mm.
Basophils	0–200 per c mm.
Eosinophils	0–400 per c mm
Reticulocytes	less than 2 per cent
Platelets	150 000–350 000 per c.mm.
Mean corpuscular haemoglobin concentration	32–36 per cent
Mean corpuscular volume	78–94 $c\mu$
Mean erythrocyte diameter	7 2 μ
Bleeding time (Duke)	2–5 minutes
Coagulation time (Lee and White)	4–7 minutes
One stage prothrombin time	12–20 seconds (varies with each batch of reagents)
Prothrombin index therapeutic range	65–35 per cent
Prothrombin concentration therapeutic range	30–10 per cent

APPENDIX

Normal Values for the Chemical Constituents of Body Fluids

C C THOMAS

Plasma or Serum

The concentrations of the electrolytes present in plasma are expressed in milliequivalents per litre (mEq/litre) a milliequivalent being a thousandth part of the equivalent weight This is useful in assessing acid base balance as one milliequivalent of any cation is exactly neutralized by one milliequivalent of any anion

Amylase (diastase)	3–16 Wohlegemuth units/ml
	71–209 Somogyi units/100 ml.
Bicarbonate	24–31 mEq/litre
Bilirubin (total)	less than 0 8 mg/100 ml
Calcium	9–11 mg/100 ml
Chloride	100–106 mEq/litre
Cholesterol (total)	150–260 mg/100 ml.
Creatine	Men 0 2–0 6 mg/100 ml women 0 35–0 9 mg
Creatinine	1–2 mg/100 ml
Gluco e (whole blood) (fasting)	60–100 mg/100 ml
Iron (serum)	0 06–0 22 mg/100 ml
Iron (whole blood)	40–55 mg/100 ml
Oxygen (whole blood)	*Saturation* Arterial 94–97 per cent
	Venous 67–77 per cent
pH	7 3–7 5
Phosphatase (alkaline)	3–13 King and Armstrong units
Phosphatase (acid)	1–5 King and Armstrong units
Inorganic phosphate (as P)	Adults 2 4–4 5 mg/100 ml. children 4–6 mg
Potassium	3 9–5 1mEq/litre
Protein	
Total	6 3–8 2 g/100 ml
Fibrinogen	0 2–0 4 g/100 ml.
Albumin	3 8–5 7 g/100 ml
Globulin	1 5–3 0 g/100 ml
A/G ratio	1 2/1–4/1
Sodium	137–147 mEq/litre
Thymol turbidity	1–4 units
Transaminase (glutamic-oxalacetic)	10–40 Cabaud units
Urea	15–40 mg/100 ml
Uric acid	2–5 mg/100 ml

Urine

Volume	1–2 litres per diem.
Specific gravity	1 010–1 025
Calcium	0·08–0 3 g per diem

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